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☐ 1. Document ID: US 6252045 B1

L7: Entry 1 of 8 File: USPT Jun 26, 2001

US-PAT-NO: 6252045
DOCUMENT-IDENTIFIER: US 6252045 B1

TITLE: Human occludin, its uses and enhancement of drug absorption using occludin inhibitors

DATE-ISSUED: June 26, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Anderson; James M.	New Haven	CT	N/A	N/A
Van Itallie; Christina M.	New Haven	CT	N/A	N/A

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Yale University	New Haven	CT	N/A	N/A	02

APPL-NO: 9/ 142732
DATE FILED: September 15, 1998

PARENT-CASE:
RELATED APPLICATION DATA This is a continuation-in-part of U.S. patent application Ser. No. 60,013,625, filed Mar. 15, 1996 which is a 371 of PCT/US97/05809 filed Mar. 14, 1997.

PCT-DATA:

APPL-NO	DATE-FILED	PUB-NO	PUB-DATE	371-DATE	102(E)-DATE
PCT/US97/05809	March 14, 1997	WO97/33605	Sep 18, 1997	Sep 15, 1998	Sep 15, 1998

INT-CL: [7] C07K 1/00
US-CL-ISSUED: 530/350; 530/324, 435/7.1
US-CL-CURRENT: 530/350; 435/7.1, 530/324
FIELD-OF-SEARCH: 530/350, 530/324, 435/7.1

PRIOR-ART-DISCLOSED:

OTHER PUBLICATIONS

Ngo et al. The Protein Folding Problem and Tertiary Structure Prediction pp.

433 & 492 & 495, 1994.

ART-UNIT: 164
PRIMARY-EXAMINER: Nolan; Patrick J.
ATTY-AGENT-FIRM: Krinsky; Mary M.

ABSTRACT:

The gene for occludin, an integral transmembrane protein specifically associated with tight junctions that functions in forming intercellular seal, is cloned, characterized, and sequenced, and the polypeptide sequence determined. Drug delivery is enhanced by administering an effective amount of occludin inhibitors. These include peptides or antibodies that interact with occludin or occludin receptors. Also included are occludin antagonists, occludin receptor components, and mixtures thereof. In some embodiments, analogues of occludin surface loops that inhibit adhesion and/or barrier properties are employed. Administration can be local or systemic; local administration in a pharmaceutically acceptable carrier is preferred in some embodiments.

18 Claims, 9 Drawing figures

☐ 2. Document ID: US 6203994 B1

L7: Entry 2 of 8 File: USPT Mar 20, 2001

US-PAT-NO: 6203994
DOCUMENT-IDENTIFIER: US 6203994 B1

TITLE: Fluorescence-based high throughput sereening assays for protein kinases and phosphatases

DATE-ISSUED: March 20, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Epps; Dennis E.	Portage	MI	N/A	N/A
Marschke; Charles K.	Kalamazoo	MI	N/A	N/A

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Pharmacia & Upjohn Company	Kalamazoo	MI	N/A	N/A	02

APPL-NO: 9/ 204335
DATE FILED: December 2, 1998

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application claims the benefit of the following provisional application: U.S. Ser. No. 60/067,833, filed Dec. 5, 1997, under 35 USC 119(e)(1).

INT-CL: [7] G01N 33/53, G01N 33/533
US-CL-ISSUED: 435/7.1; 435/4, 435/6, 435/7.6, 435/7.71, 435/7.92, 435/7.93, 435/7.94, 435/7.95, 435/18, 435/21, 435/183 , 435/968, 436/546, 436/547, 436/800

US-CL-CURRENT: 435/7.1; 435/18, 435/183, 435/21, 435/4, 435/6, 435/7.6, 435/7.71, 435/7.92, 435/7.93, 435/7.94, 435/7.95 , 435/968, 436/546, 436/547, 436/800
FIELD-OF-SEARCH: 435/4, 435/6, 435/7.1, 435/7.6, 435/7.71, 435/7.92-7.95, 435/18, 435/21, 435/183, 435/968, 436/546, 436/547, 436/800

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
4681859	July 1987	Kramer	436/501
5070025	December 1991	Klein et al.	436/546

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
WO 93/03377	February 1993	WOX	
WO 95/18823	July 1995	WOX	
WO 97/42501	November 1997	WOX	
WO 98/18956	May 1998	WOX	

OTHER PUBLICATIONS

Dandliker, W.B. et al., "Equilibrium and Kinetic Inhibition Assays Based Upon Fluorescence Polarization," Methods in Enzymology, 74:3-28 (1981);.
Owicki, J.C. et al., "Application of Fluorescence Polarization Assays in High-Throughput Screening," Genetic Engineering News, 17:27 (1997);.
Krishna Seethala, "A Fluorescence Polarization Tyrosine Kinase Assay for High Throughput Screening," 3rd Annual Conference of The Society for Biomolecular Screening, San Diego, CA, Sep. 22-25, 1997;.
Checovich, W.J. et al., Nature, 375:254-256 (1995);.
T. Hunter, Cell, 80:225-236 (1995);.
Levine, L.M. et al., Anal. Biochem., 247:83-88 (1997);.
Rotman, B. et al., Proc. Nat. Acad. Sci., 50:1-6 (1963);.
Zhang, Z-Y, et al., Analytical Biochemistry, 211:7-15 (1993).

ART-UNIT: 161
PRIMARY-EXAMINER: Le; Long V.
ASSISTANT-EXAMINER: Do; Pensee T.
ATTY-AGENT-FIRM: Rehberg; Edward F. Kerber; Lori L.

ABSTRACT:

The invention relates to novel fluorescence-based assays for protein kinases and phosphatases which can be used in high throughput screening. The methods of the invention utilize a competitive immunoassay to determine the amount of substrate that is phosphorylated or dephosphorylated during the course of a kinase or phosphatase reaction to yield a product, as well as the phosphorylating or dephosphorylating activity of a kinase or phosphatase.

33 Claims, 16 Drawing figures

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 3. Document ID: US 6074846 A

L7: Entry 3 of 8 File: USPT Jun 13, 2000

US-PAT-NO: 6074846
DOCUMENT-IDENTIFIER: US 6074846 A

TITLE: Hepatitis C virus asialoglycoproteins

DATE-ISSUED: June 13, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ralston; Robert O.	Danville	CA	N/A	N/A
Marcus; Frank	Danville	CA	N/A	N/A
Thudium; Kent B.	Oakland	CA	N/A	N/A
Gervase; Barbara A.	Vallejo	CA	N/A	N/A
Hall; John A.	Rohnert Park	CA	N/A	N/A
Berger; Kim M.	Lafayette	CA	N/A	N/A
Choo; Oui-Lim	El Cerrito	CA	N/A	N/A
Houghton; Michael	Danville	CA	N/A	N/A
Kuo; George	San Francisco	CA	N/A	N/A

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Chiron Corporation	Emeryville	CA	N/A	N/A	02

APPL-NO: 8/ 442805
DATE FILED: May 17, 1995

PARENT-CASE:
RELATED APPLICATIONS This application is a Divisional of copending U.S. Ser. No. 08/249,843, filed May 26, 1994, which is a continuation-in-part of U.S. Ser. No. 07/758,880, filed Sep. 13, 1991, abandoned, which is a continuation-in-part of U.S. Ser. No. 07/611,419, filed Nov. 8, 1990, now abandoned, the discosures of which are incorporated herein by reference.

INT-CL: [7] C12P 21/02, C12Q 1/70, A61K 39/29, C07K 1/00
US-CL-ISSUED: 435/69.3; 435/5, 435/69.9, 424/185.1, 424/228.1, 530/395, 530/820

US-CL-CURRENT: 435/69.3; 424/185.1, 424/228.1, 435/5, 435/69.9, 530/395, 530/820
FIELD-OF-SEARCH: 435/5, 435/69.9, 435/69.3, 424/185.1, 424/228.1, 530/395, 530/820

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
5135854	August 1992	MacKay et al.	N/A
5350671	September 1994	Houghton et al.	435/5

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
0 318 216 A1	May 1989	EPX	
0 320 267	June 1989	EPX	
0 388 232 A1	September 1990	EPX	
WO 91/15771	October 1991	WOX	
92/08734	May 1992	WOX	

OTHER PUBLICATIONS

Lanford et al., "Analysis of Hepatitis C Virus Capsid, E1, and E2/NS1 Proteins Expressed in Insect Cells," Virology 197:225-235 (1993).
Spaete et al., "Characterization of the Hepatitis C Virus E2/NS1 Gene Product Expressed in Mammalian Cells," Virology 188:819-830 (1992).
Saunders Dictionary & Encyclopedia of Laboratory Medicine and Technology p. 138 (1987).
Hedo, "Lectins as Tools . . . ," Receptor Purification Procedures (Alan R Liss,)NY) pp. 45-60 (1984).
Goochee et al., "The Oligosccharides of glycoproteins . . . , " Biotechnology 9:1347-1355 (1991).

ART-UNIT: 163
PRIMARY-EXAMINER: Woodward; Michael P.
ASSISTANT-EXAMINER: Zeman; Mary K.
ATTY-AGENT-FIRM: Robins & Associates Harbin; Alisa A. Blackburn; Robert P.

ABSTRACT:

Two Hepatitis C Virus envelope proteins (E1 and E2) are expressed without sialylation. Recombinant expression of these proteins in lower eukaryotes, or in mammalian cells in which terminal glycosylation is blocked, results in recombinant proteins which are more similar to native HCV glycoproteins. When isolated by GNA lectin affinity, the E1 and E2 proteins aggregate into virus-like particles.

9 Claims, 0 Drawing figures

☐ 4. Document ID: US 6074852 A

L7: Entry 4 of 8 File: USPT Jun 13, 2000

US-PAT-NO: 6074852
DOCUMENT-IDENTIFIER: US 6074852 A

TITLE: Hepatitis C virus asialoglycoproteins

DATE-ISSUED: June 13, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ralston; Robert O.	Danville	CA	N/A	N/A
Marcus; Frank	Danville	CA	N/A	N/A
Thudium; Kent B.	Oakland	CA	N/A	N/A
Gervase; Barbara A.	Vallejo	CA	N/A	N/A
Hall; John A.	Rohnert Park	CA	N/A	N/A
Berger; Kim M.	Lafayette	CA	N/A	N/A
Choo; Qui-Lim	El Cerrito	CA	N/A	N/A
Houghton; Michael	Danville	CA	N/A	N/A
Kuo; George	San Francisco	CA	N/A	N/A

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Chiron Corporation	Emeryville	CA	N/A	N/A	02

APPL-NO: 8/ 443900
DATE FILED: May 17, 1995

PARENT-CASE:
RELATED APPLICATIONS This application is a divisional of application Ser. No. 08/249,843, filed May 26, 1994, which is a continuation-in-part of U.S. Ser. No. 07/758,880, filed Sep. 13, 1991, now abandoned which is a continuation-in-part of U.S. Ser. No. 07/611,419, filed Nov. 8, 1990, now abandoned, the discosures of which are incorporated herein by reference.

INT-CL: [7] C12Q 1/70, C12P 21/04, A61K 39/29
US-CL-ISSUED: 435/69.9; 435/5, 424/185.1, 424/228.1, 530/395, 530/826
US-CL-CURRENT: 435/69.9; 424/185.1, 424/228.1, 435/5, 530/395, 530/826
FIELD-OF-SEARCH: 435/5, 435/69.9, 424/185.1, 424/228.1, 530/395, 530/826

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
5350571	September 1994	Houghton et al.	435/5

OTHER PUBLICATIONS

Rudolph et al., "The Yeast Secretory Pathway . . . ," Cell 58:133-145 (1989).
Sleep et al., "The Secretion of Human Serum . . . ," Bio/Techology 8: 42-46 (1990).
Goochu et al., "The Oligosaccharides of Glycoproteins:," Bio/Technology 9: 1347-1355 (1991).
Saunders Dictionary & Encyclopedia of Laboratory Medicine and Technololgy, p. 138 (1987).

ART-UNIT: 163
PRIMARY-EXAMINER: Wortman; Donna C.
ASSISTANT-EXAMINER: Zeman; Mary K
ATTY-AGENT-FIRM: Robins; Roberta L. Harbin; Alisa A. Blackburn; Robert P.

ABSTRACT:

Two Hepatitis C Virus envelope proteins (E1 and E2) are expressed without sialylation. Recombinant expression of these proteins in lower eukaryotes, or in mammalian cells in which terminal glycosylation is blocked, results in recombinant proteins which are more similar to native HCV glycoproteins. When isolated by GNA lectin affinity, the E1 and E2 proteins aggregate into

virus-like particles.

11 Claims, 0 Drawing figures

☐ 5. Document ID: US 5942234 A

L7: Entry 5 of 8 File: USPT Aug 24, 1999

US-PAT-NO: 5942234
DOCUMENT-IDENTIFIER: US 5942234 A

TITLE: Hepatitis C virus asialoglycoproteins

DATE-ISSUED: August 24, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ralston; Robert O.	Danville	CA	N/A	N/A
Marcus; Frank	Danville	CA	N/A	N/A
Thudium; Kent B.	Oakland	CA	N/A	N/A
Gervase; Barbara A.	Vallejo	CA	N/A	N/A
Hall; John A.	Rohnert Park	CA	N/A	N/A
Berger; Kim M.	Lafayette	CA	N/A	N/A
Choo; Qui-Lim	El Cerrito	CA	N/A	N/A
Houghton; Michael	Danville	CA	N/A	N/A
Kuo; George	San Francisco	CA	N/A	N/A

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Chiron Corporation	Emeryville	CA	N/A	N/A	02

APPL-NO: 8/ 443260
DATE FILED: May 17, 1995

PARENT-CASE:
RELATED APPLICATIONS This application is a divisional, of application Ser. No. 08/249,843, filed May 26, 1994, which is a continuation-in-part of U.S. Ser. No. 07/758,880, filed Sep. 13, 1991, abandoned, which is a continuation-in-part of U.S. Ser. No. 07/611,419, filed Nov. 8, 1990, now abandoned, the discosures of which are incorporated herein by reference.

INT-CL: [6] F61K 39/29, C12P 21/62, C12Q 1/70, C07K 1/00
US-CL-ISSUED: 424/228.1; 424/185.1, 435/5, 435/69.2, 435/69.9, 530/395, 530/826

US-CL-CURRENT: 424/228.1; 424/185.1, 435/5, 435/69.2, 435/69.9, 530/395, 530/826
FIELD-OF-SEARCH: 435/5, 435/69.9, 435/69.3, 424/185.1, 424/228.1, 530/395, 530/826

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
5350671	September 1994	Houghton et al.	435/5

OTHER PUBLICATIONS

Lanford et al., "Analysis of Hepatitis C Virus Capsid, E1, and E2/NS1 Proteins Expressed in Insect Cells," Virology 197:225-235 (1993).
Spaete et al., "Characterization of the Hepatitis C Virus E2/NS1 Gene Product Expressed in Mammalian Cells," Virology 188:819-830 (1992).
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Farci et al., "Lack of protective immunity against reinfection with Hepatitis C virus," Science 258:135-140 (1992).
Saunders Dictionary & Encyclopedia of Laboratory Medicine and Technology (W.B. Saunders Company, Philadelphia) p. 138 (1987).
Goochee et al., "The oligosaccharides of glycoproteins: bioprocess factors affecting oligosaccharide structure and their effect on glycoprotein properties," Bio/Technology 9:1347-1353 (1991).

ART-UNIT: 163
PRIMARY-EXAMINER: Woodward; Michael P.
ASSISTANT-EXAMINER: Zeman; Mary K
ATTY-AGENT-FIRM: Robins & Associates Harbin; Alisa A. Blackburn; Robert P.

ABSTRACT:

Two Hepatitis C Virus envelope proteins (E1 and E2) are expressed without sialylation. Recombinant expression of these proteins in lower eukaryotes, or in mammalian cells in which terminal glycosylation is blocked, results in recombinant proteins which are more similar to native HCV glycoproteins. When isolated by GNA lectin affinity, the E1 and E2 proteins aggregate into virus-like particles.

27 Claims, 0 Drawing figures

☐ 6. Document ID: US 5880334 A

L7: Entry 6 of 8 File: USPT Mar 9, 1999

US-PAT-NO: 5880334
DOCUMENT-IDENTIFIER: US 5880334 A

TITLE: DNA encoding phosphoenolpyruvate carboxykinase, recombinant vector and transformed plant containing the same

DATE-ISSUED: March 9, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Suzuki; Shoichi	Shizuoka	N/A	N/A	JPX
Arai; Masao	Shizuoka	N/A	N/A	JPX
Murai; Nobuhiko	Shizuoka	N/A	N/A	JPX
Finnegan; Patrick M.	Canberra	N/A	N/A	AUX
Burnell; James Nigel	Queensland	N/A	N/A	AUX

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Japan Tobacco Inc.	Tokyo	N/A	N/A	JPX	03

APPL-NO: 8/ 617801
DATE FILED: May 8, 1996

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
JP	180756	July 9, 1994
JP	136000	May 10, 1995

PCT-DATA:

APPL-NO	DATE-FILED	PUB-NO	PUB-DATE	371-DATE	102(E)-DATE
PCT/JP95/01356	July 6, 1995	WO96/01895	Jan 25, 1996	May 8, 1996	May 8, 1996

INT-CL: [6] A01H 5/00, C12N 15/82, C12N 15/63, C07H 21/04
US-CL-ISSUED: 800/298; 435/320.1, 536/23.6, 800/320.2
US-CL-CURRENT: 800/298; 435/320.1, 536/23.6, 800/320.2
FIELD-OF-SEARCH: 435/320.1, 536/23.6, 800/205, 800/DIG.57

PRIOR-ART-DISCLOSED:

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
0507698	October 1992	EPX	
WO94-00977	January 1994	WOX	

OTHER PUBLICATIONS

Kim et al. Molecular cloning of cucumber phosphoenolpyruvate carboxykinase and developmental regulation of gene expression. Plant Molecular Biology. 26:423-434, Oct. 1994.
Osteras et al. Molecular and expression analysis of the Rhizobium meliloti phosphoenolpyruvate carboxykinase (pckA) gene. Journal of Bacteriology. 177(6):1452-1460, Mar. 1995.
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Medina et al. Sequence of the pckA gene of Escherichia coli K-12: relevance to genetic and allosteric regulation and homology of E. coli phosphoenolpyruvate carboxykinase with the enzymes from Trypanosoma brucei and Saccharomyces cerevisiae. Journal of, Dec. 1990.
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Hudspeth et al. Structure and expression of the maize gene encoding the phosphoenolpyruvate carboxykinase isozyme involved in C4 photosynthesis. Plant Molecular Biology, 12:579-589, 1989.
R. Hudspeth et al, "Structure and Expression of the Maize Gene Encoding the Phosphoenolpyruvate Carboxylase Isozyme Involved in C4 Photosynthesis", Plant Molecular Biology, vol. 12, 1989, pp. 579-589.
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Derwent WPI English Abstract of Japanese Patent 4-222527.
Chih-ching, Plant Tissue Culture, Pitman Publishing Inc., pp. 43-51 (1981).
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Murashige et al, Physiologia Plantarum, vol. 15, pp. 473-497 (1962).
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Henikoff, Gene, vol. 28, pp. 351-359 (1984).
Burnell, Aust. J. Plant. Physiol., vol. 13, pp. 577-587 (1986).
Baba et al, Plant Cell Physiol., vol. 27, No. 3, pp. 463-471 (1986).
Tada et al, Theor Appl Genet, vol. 80, pp. 475-480 (1990).
Yie et al, Nucleic Acids Research, vol. 21, No. 2, p. 361 (1993).
Kyte et al, J. Mol. Biol., vol. 157, pp. 105-132 (1982).
Derwent WPI English Abstract of European Patent 504869.

ART-UNIT: 169
PRIMARY-EXAMINER: Robinson; Douglas W.
ASSISTANT-EXAMINER: Wai; Thanda
ATTY-AGENT-FIRM: Birch, Stewart, Kolasch & Birch, LLP

ABSTRACT:

A cloned DNA encoding phosphoenolpyruvate carboxykinase of a C.sub.4 plant is disclosed. The DNA according to the present invention encodes the amino acid sequence shown in SEQ ID NOS: 1-6 in Sequence Listing or the same amino acid sequence as shown in SEQ ID NOS: 1-6 except that one or more amino acid is added, deleted, inserted or substituted, with the proviso that the polypeptide having this amino acid sequence has phosphoenolpyruvate carboxykinase activity.

13 Claims, 5 Drawing figures

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 7. Document ID: US 5246835 A

L7: Entry 7 of 8 File: USPT Sep 21, 1993

US-PAT-NO: 5246835
DOCUMENT-IDENTIFIER: US 5246835 A

TITLE: Method of diagnosing renal diseases

DATE-ISSUED: September 21, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Suzuki; Hirokazu	Kanagawa	N/A	N/A	JPX
Sakurai; Yoshinori	Sagamihara	N/A	N/A	JPX
Ohashi; Yoshitami	Hatano	N/A	N/A	JPX
Goto; Masayoshi	Isehara	N/A	N/A	JPX

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Wakamoto Pharmaceutical Co., Ltd.	Tokyo	N/A	N/A	JPX	03

APPL-NO: 7/ 887154
DATE FILED: May 22, 1992

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
JP	3-148080	May 24, 1991
JP	4-105214	April 1, 1992

INT-CL: [5] G01N 33/543, G01N 33/68
US-CL-ISSUED: 435/7.95; 435/7.5, 435/7.92, 436/63, 436/86, 436/166, 436/169, 436/513, 436/516, 436/811
US-CL-CURRENT: 435/7.95; 435/7.5, 435/7.92, 436/166, 436/169, 436/513, 436/516, 436/63, 436/811, 436/86
FIELD-OF-SEARCH: 436/166, 436/169, 436/86, 436/63, 436/516, 436/811, 436/513, 435/7.9, 435/7.92, 435/7.95, 435/7.5

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
5139932	August 1992	Cederholm et al.	435/7.95

OTHER PUBLICATIONS

Blatant et al., Curr. Probe. Clin. Biochem. (1979) 9:216-234.
Wiggins et al., Clin. Chim Acta (1985) 149:155-163.
Pharmacia (1982) Isoelectrifocusing, p. 1-5.
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ART-UNIT: 182
PRIMARY-EXAMINER: Ceperley; Mary E.
ATTY-AGENT-FIRM: Burns, Doane, Swecker & Mathis

ABSTRACT:

A method of diagnosing renal diseases by detecting fragments of albumin in human urine. The detection of the fragments is carried out by, for example, immunological methods or liquid chromatography techniques.

19 Claims, 15 Drawing figures

☐ 8. Document ID: WO 200035483 A1

L7: Entry 8 of 8 File: DWPI Jun 22, 2000

DERWENT-ACC-NO: 2000-442276
DERWENT-WEEK: 200038

applicant

TITLE: Inhibition of lectin complement pathway (LCP)-associated complement activation with a monoclonal antibody to a mannose binding lectin (MBL) ligand, useful for treating disorders such as arthritis

INVENTOR: COLLARD, C D; STAHL, G L

PATENT-ASSIGNEE: BRIGHAM & WOMENS HOSPITAL INC (BGHM)

PRIORITY-DATA: 1998US-0112390 (December 15, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 200035483 A1	June 22, 2000	E	064	A61K039/395

DESIGNATED-STATES: CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
WO 200035483A1	December 15, 1999	1999WO-US29919	N/A

INT-CL (IPC): A61K 39/395; C12N 5/06; C12N 5/16

ABSTRACTED-PUB-NO: WO 200035483A
BASIC-ABSTRACT:

NOVELTY - A method (M1) for inhibiting lectin complement pathway (LCP)-associated complement activation, comprising contacting a mammalian cell

having surface exposed mannose binding lectin (MBL) ligand with an MBL inhibitor to inhibit LCP-associated complement activation, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a composition comprising an MBL inhibitor, where the MBL inhibitor is an isolated binding peptide that selectively binds to a human MBL epitope and inhibits LCP associated complement activation;

(2) hybridoma cell lines deposited under ATCC HB-12621, HB-12620, and HB-12619; and

(3) a method (M2) for screening a cell for susceptibility to treatment with an MBL inhibitor comprising detecting the presence of a MBL on a surface of a mammalian cell, where the presence of the MBL indicates susceptibility to LCP associated complement activation and treatment with an MBL inhibitor.

ACTIVITY - Cardiant; antiarthritis; vasotropic; cerebroprotective; dermatological, immunosuppressive, antiinflammatory; respiratory.

MECHANISM OF ACTION - MBL inhibitors inhibit LCP-associated complement activation.

In order to demonstrate specifically the role of MBL in complement activation following oxidative stress of human endothelial cells, MBL and C3 deposition on hypoxic human endothelial cells following reoxygenation in human sera was assessed. To demonstrate the complement inhibitory action of these anti-human MBL monoclonal antibodies (mAbs), hypoxic HUVECs (human umbilical vein endothelial cells) were reoxygenated in human sera treated with PBS (phosphate buffered saline) (vehicle), 3F8, hMBLI.2, 2A9, or IC10 (50 micro g/ml final concentration). Cell membrane bound proteins were resolved by SDS-PAGE (sodium dodecyl sulfate-polyacrylamide gel electrophoresis) under reduced conditions, transferred to membranes, and analyzed for human C3dg (i.e., part of the alpha -chain of iC3b). The alpha and beta -chain of iC3b were the only C3 stainable bands present on the cellular membranes. A representative C3dg band for vehicle, 3F8-, hMBLI.2-, 2A9- and IC10-treated cells was observed. A significant decrease in C3dg band intensity on cells reoxygenated in human sera treated with either 3F8, 2A9 or hMBL1.2 was observed. However, the non-functional clone, IC10, did not decrease iC3b deposition (i.e., C3dg band intensity) on the endothelial membranes. These data supported the role of MBL-dependent complement activation following reoxygenation of hypoxic HUVECs. Further, the data confirmed that clone IC10 is an isotype control mAb that does not functionally inhibit MBL. Dual labeling for MBL and C3 deposition on normoxic and hypoxic HUVECs was performed to demonstrate co-localization of these complement components and MBL-dependent complement pathway activation. Normoxic and hypoxic HUVECs were reoxygenated in 30% HS (not defined) treated with and without mAb 3F8 (5 micro g/ml) or IC10 (50 micro g/ml). MBL (blue), C3 (green) and nuclei (red) were then stained on the same slide and analyzed by immunofluorescent confocal microscopy. Small amounts of C3 and MBL staining were observed under normoxic conditions. C3 and MBL staining on hypoxic/reoxygenated HUVECs was significantly greater than normoxic HUVECS. Clone IC10 failed to inhibit C3 or MBL deposition following oxidative stress. C3 and MBL staining was significantly decreased on hypoxic/reoxygenated HUVECs treated with mAb 3F8 (5 micro g/ml) to levels below those observed under normoxic conditions (similar results were observed with mAbs hMBL1.2 or 2A9). The data demonstrated that functional inhibition of MBL with a mAb attenuates C3 deposition following oxidative stress of human endothelial cells.

USE - Inhibition of complement associated activation is useful for the treatment of disorders such as arthritis, myocardial infarction, ischemia, reperfusion, transplantation, CPB (not defined), stroke, acute respiratory diseases (ARDs), systemic lupus erythematosus (SLE), lupus, and dialysis.

ABSTRACTED-PUB-NO: WO 200035483A
EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/9

DERWENT-CLASS: B04 D16
CPI-CODES: B04-F05; B04-G01; B04-G21; B11-C08E; B12-K04E; B14-C03; B14-C09; B14-F01; B14-G02; B14-K01; B14-N16; B14-N17; D05-H09; D05-H11A1; D05-H15;

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Terms	Documents
((MBL) or (mannose adj binding adj lectin))near (antibod$)	8

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starting with: INHIBIT$(INHIBIT-RATHER).P28-P87,P89-P89,P23-P27,P20-P22,P1-P18.

Search Results -

Terms	Documents
((MBL) or (mannose adj binding adj lectin))near ((LCM) or (lectin complement adj pathway)) near (inhibit$)	0

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Refine Search: ((MBL) or (mannose adj binding adj lectin))near ((LCM) or (lectin complement adj pathway)) near (inhibit$) Clear

Search History

Today's Date: 7/17/2001

DB Name	Query	Hit Count	Set Name
USPT,PGPB,JPAB,EPAB,DWPI	((MBL) or (mannose adj binding adj lectin))near ((LCM) or (lectin complement adj pathway)) near (inhibit$)	0	L8
USPT,PGPB,JPAB,EPAB,DWPI	((MBL) or (mannose adj binding adj lectin))near ((LCM) or (lectin complement adj pathway))	176	L7
USPT,PGPB,JPAB,EPAB,DWPI	((MBL) or (mannose adj binding adj lectin))near (antibod$)	8	L6
USPT	(MHC ADJ CLASS ADJ II) same (chimeric or hetero$ or dimeri$)	28	L5
USPT	(MHC ADJ CLASS ADJ II) near (fusion or chimeric or hetero$ or dimeri$)	4	L4
USPT	(MHC ADJ CLASS ADJ II) near (fusion or chimeric or hetero$) near (dimeri$)	0	L3
USPT	(MHC ADJ CLASS ADJ II) near (fusion or chimeric or hetero$) near (antibod$ or protein)	3	L2
USPT	(MHC ADJ CLASS ADJ II) near (fusion or chimeric or hetero$) near (antibod$ or protein)	3	L1

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NEWS 2	Dec 17	The CA Lexicon available in the CAPLUS and CA files
NEWS 3	Feb 06	Engineering Information Encompass files have new names
NEWS 4	Feb 16	TOXLINE no longer being updated
NEWS 5	Apr 23	Search Derwent WPINDEX by chemical structure
NEWS 6	Apr 23	PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS 7	May 07	DGENE Reload
NEWS 8	Jun 20	Published patent applications (A1) are now in USPATFULL
NEWS 9	JUL 13	New SDI alert frequency now available in Derwent's DWPI and DPCI

NEWS EXPRESS	July 11 CURRENT WINDOWS VERSION IS V6.0b, CURRENT MACINTOSH VERSION IS V5.0C (ENG) AND V5.0JB (JP), AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2001
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L1 0 MBL (5N) (ANTIBOD)

=> ((MBL) or (Mannose binding lectin)) (10N) (antibod?
((MBL) IS NOT A RECOGNIZED COMMAND
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=> ((MBL) or (Mannose binding lectin)) (10N) (antibod?)
((MBL) IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s ((MBL) or (Mannose binding lectin)) (10N) (antibod?)
L2 107 ((MBL) OR (MANNOSE BINDING LECTIN)) (10N) (ANTIBOD?)

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 47 DUP REM L2 (60 DUPLICATES REMOVED)

=> s l3 (P) ((LCP) or (lectin complement pathway))
L4 6 L3 (P) ((LCP) OR (LECTIN COMPLEMENT PATHWAY))

=> dis l4 1-6 ibib abs kwic

L4 ANSWER 1 OF 6 MEDLINE
ACCESSION NUMBER: 2001209693 MEDLINE
DOCUMENT NUMBER: 21195380 PubMed ID: 11298833
TITLE: Isolation, cloning and functional characterization of porcine mannose-binding lectin.
AUTHOR: Agah A; Montalto M C; Young K; Stahl G L
CORPORATE SOURCE: Center for Experimental Therapeutics and Reperfusion Injury, Department of Anesthesiology, Perioperative and Pain Medicine, Brigham & Women's Hospital, Harvard Medical School, Boston, MA 02115, USA.
CONTRACT NUMBER: HL52886 (NHLBI)
SOURCE: IMMUNOLOGY, (2001 Mar) 102 (3) 338-43.
Journal code: GH7; 0374672. ISSN: 0019-2805.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517

Last Updated on STN: 2001
Entered Medline: 20010510

AB Binding of mannose-binding lectin (MBL), a C-type lectin, and its associated serine proteases, MASP-1 and MASP-2, to cell surface carbohydrates activates the **lectin complement pathway**. As MBL plays an important role in innate immunity, it has been cloned and characterized in several species. While the pig may be used as a source of organs/tissues for xenotransplantation, little is known about its MBL, thus, we report the isolation of three monomeric forms of MBL from porcine serum. Sodium dodecyl sulphate-polyacrylamide gel electrophoresis and Coomassie staining of reduced porcine MBL revealed the presence of three monomeric forms with approximate molecular masses of 30 000, 32 000 and 34 000. Protein sequencing identified these monomeric forms as one single protein, suggesting post-translational modification. Western blot analysis demonstrated the cross-reactivity of anti-human **MBL** polyclonal **antibody** with porcine **MBL**. A full-length porcine liver **MBL** cDNA was isolated and the predicted amino acid sequence exhibited 64.9% identity with human MBL and 50.2% and 56.7% identity with rat A and C MBL, respectively. Furthermore, Northern blot analysis demonstrated the presence of a single (approximately 1.4-1.6 kilobase pair) transcript in porcine liver. Addition of purified porcine MBL to MBL-deficient human sera augmented N-acetylglucosamine inhibitable C3 deposition to mannan-coated plates in a dose-dependent manner. Taken together, these data demonstrate that porcine and human MBL are highly conserved, sharing structural and functional characteristics.

AB . . . mannose-binding lectin (MBL), a C-type lectin, and its associated serine proteases, MASP-1 and MASP-2, to cell surface carbohydrates activates the **lectin complement pathway**. As MBL plays an important role in innate immunity, it has been cloned and characterized in several species. While the. . . sequencing identified these monomeric forms as one single protein, suggesting post-translational modification. Western blot analysis demonstrated the cross-reactivity of anti-human **MBL** polyclonal **antibody** with porcine **MBL**. A full-length porcine liver **MBL** cDNA was isolated and the predicted amino acid sequence exhibited 64.9% identity with human MBL and 50.2% and 56.7% identity. . .

L4 ANSWER 2 OF 6 MEDLINE
ACCESSION NUMBER: 2000255148 MEDLINE
DOCUMENT NUMBER: 20255148 PubMed ID: 10793066
TITLE: Complement activation after oxidative stress: role of the lectin complement pathway.
AUTHOR: Collard C D; Vakeva A; Morrissey M A; Agah A; Rollins S A; Reenstra W R; Buras J A; Meri S; Stahl G L
CORPORATE SOURCE: Center for Experimental Therapeutics and Reperfusion Injury, Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA.
CONTRACT NUMBER: HL-03854 (NHLBI)
HL-52886 (NHLBI)
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (2000 May) 156 (5) 1549-56.
Journal code: 3RS; 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000616
Last Updated on STN: 20000616
Entered Medline: 20000602

AB The complement system plays an important role in mediating tissue injury after oxidative stress. The role of mannose-binding lectin (MBL) and the **lectin complement pathway** (**LCP**) in mediating complement activation after endothelial oxidative stress was investigated. iC3b deposition on hypoxic (24 hours; 1% O(2))/reoxygenated (3 hours; 21% O(2)) human endothelial cells was attenuated by N-acetyl-D-glucosamine or D-mannose, but not L-mannose, in a dose-dependent manner. Endothelial iC3b deposition after oxidative stress was also attenuated in **MBL**-deficient serum. Novel, functionally inhibitory, anti-human **MBL** monoclonal **antibodies** attenuated **MBL**-dependent C3 deposition on mannan-coated plates in a dose-dependent manner. Treatment of human serum with anti-**MBL** monoclonal **antibodies** inhibited **MBL** and C3 deposition after endothelial oxidative stress. Consistent with our in vitro findings, C3 and MBL immunostaining throughout the ischemic area at risk increased during rat myocardial reperfusion in vivo. These data suggest that the **LCP** mediates complement activation after tissue oxidative stress. Inhibition of MBL may represent a novel therapeutic strategy for ischemia/reperfusion injury and other complement-mediated disease states.

AB . . . system plays an important role in mediating tissue injury after oxidative stress. The role of mannose-binding lectin (MBL) and the **lectin complement pathway** (**LCP**) in mediating complement activation after endothelial oxidative stress was investigated. iC3b deposition on hypoxic (24 hours; 1% O(2))/reoxygenated (3 hours;. . . N-acetyl-D-glucosamine or D-mannose, but not L-mannose, in a dose-dependent manner. Endothelial iC3b deposition after oxidative stress was also attenuated in **MBL**-deficient serum. Novel, functionally inhibitory, anti-human **MBL** monoclonal **antibodies** attenuated **MBL**-dependent C3 deposition on mannan-coated plates in a dose-dependent manner. Treatment of human serum with anti-**MBL** monoclonal **antibodies** inhibited **MBL** and C3 deposition after endothelial oxidative stress. Consistent with our in vitro findings, C3 and MBL immunostaining throughout the ischemic area at risk increased during rat myocardial reperfusion in vivo. These data suggest that the **LCP** mediates complement activation after tissue oxidative stress. Inhibition of MBL may represent a novel therapeutic strategy for ischemia/reperfusion injury and. . .

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:137043 CAPLUS
DOCUMENT NUMBER: 134:188227
TITLE: Inhibitors of the lectin complement pathway (LCP) and their use
INVENTOR(S): Stahl, Gregory L.; Lekowski, Robert
PATENT ASSIGNEE(S): The Brigham and Women's Hospital, Inc., USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012212	A1	20010222	WO 2000-US22123	20000814

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-148815 P 19990813

AB The invention relates to methods and products for regulating lectin complement pathway assocd. complement activation. The methods include both in vitro and in vivo methods for inhibiting lectin complement pathway assocd. complement activation. The methods are accomplished by contacting a mammalian cell having surface exposed MBL ligand with an effective amt. of a mannan binding lectin (MBL) receptor antagonist to inhibit lectin complement pathway assocd. complement activation. The mannan binding lectin receptor antagonist may be administered to a subject to prevent cellular injury mediated by lectin complement pathway assocd. complement activation. The products of the invention include compns. of a mannan binding lectin receptor antagonist. The mannan binding lectin receptor antagonist is an isolated mannan binding lectin that selectively binds to a human mannan binding lectin epitope and that inhibits lectin complement pathway assocd. complement activation.

REFERENCE COUNT: 9

REFERENCE(S):

(1) Brigham & Womens Hospital; WO 0035483 A 2000 CAPLUS
(5) Holtzhauer, M; WO 9939209 A 1999 CAPLUS
(7) Lhotta, K; NEPHROLOGY, DIALYSIS, TRANSPLANTATION 1999, V14(4), P881 MEDLINE
(8) Shikhman, A; JOURNAL OF IMMUNOLOGY 1994, V153(12), P5593 CAPLUS
(9) Turner, M; IMMUNOLOGY TODAY 1996, V17(11), P532 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Keratins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(1, as mannan-binding lectin receptor; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin **antibody** as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LAA-I (Laburnum alpinum I); mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin **antibody** as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(UEA-II (Ulex europaeus II); mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin **antibody** as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Complement
(activation, lectin pathway; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin **antibody** as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Respiratory distress syndrome
(adult, inhibition of cellular injury from; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin **antibody** as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Drug delivery systems
(aerosols; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin **antibody** as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-H(O) CSA-1 (Cytisus sessilifolius 1); mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin **antibody** as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Cytisus sessilifolius
(anti-H(O) lectin 1 (CSA-1) of; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin **antibody** as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Keratins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**antibodies** to; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin **antibody** as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Heart, disease
(infarction, inhibition of cellular injury from; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin **antibody** as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Arthritis
Atherosclerosis
Cardiopulmonary bypass
Dialysis
Ischemia
Lupus erythematosus
Transplant and Transplantation
(inhibition of cellular injury from; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin **antibody** as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Reperfusion
Respiratory tract
(injury, inhibition of cellular injury from; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or

anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Laburnum alpinum
(lectin LAA-I of; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Ulex europaeus
(lectin UEA-II of; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(lectin, mannan-binding; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Legume (Fabaceae)
(lectins of; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(legume-derived; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Drug delivery systems
(localized; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Cytoprotective agents
Drug screening
(mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Structure-activity relationship
(mannan-binding lectin receptor antagonist of peptides; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Peptide library
(mannan-binding lectin receptor antagonists; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(mannan-binding lectin receptor antagonists; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Agglutinins and Lectins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(mannan-binding, treatment of disorders mediated by; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Brain, disease
(stroke, inhibition of cellular injury from; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Lupus erythematosus
(systemic, inhibition of cellular injury from; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Antibodies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to keratin; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT 160071-01-2 160071-68-1 160071-69-2 160071-70-5 160071-71-6
160071-76-1 160071-77-2 160071-78-3 160071-79-4 160071-83-0
160071-84-1 160071-85-2 160071-86-3 160071-87-4
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(mannan-binding lectin receptor antagonist; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:420986 CAPLUS
DOCUMENT NUMBER: 133:57580
TITLE: Methods and products for regulating lectin complement pathway associated complement activation
INVENTOR(S): Stahl, Gregory L.; Collard, Charles D.
PATENT ASSIGNEE(S): Brigham and Women's Hospital, Inc., USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035483	A1	20000622	WO 1999-US29919	19991215
W: CA, JP				

RW: AT, BE, CH, CY, DE, DK, ES, FI, B, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1998-112390 P 19981215

AB The invention relates to methods and products for regulating lectin complement pathway assocd. complement activation. The methods include both in vitro and in vivo methods for inhibiting lectin complement pathway assocd. complement activation. The methods are accomplished by contacting a mammalian cell having surface exposed MBL ligand with an effective amt. of a mannan binding lectin inhibitor to inhibit lectin complement pathway assocd. complement activation. The mannan binding lectin inhibitor may be administered to a subject to prevent cellular injury mediated by lectin complement pathway assocd. complement activation. The products of the invention include compns. of a mannan binding lectin inhibitor. The mannan binding lectin inhibitor is an isolated mannan binding lectin binding peptide that selectively binds to a human mannan binding lectin epitope and that inhibits lectin complement pathway assocd. complement activation. The products also include hybridoma cell lines and pharmaceutical compns.

REFERENCE COUNT: 4

REFERENCE(S):
(1) Endo; International Immunology 1996, V8(9), P1355 CAPLUS
(2) Endo; Journal of Immunology 1998, V161, P4924 CAPLUS
(3) Sato; International Immunology 1994, V6(4), P665 CAPLUS
(4) Thiel; Nature 1997, V386, P506 CAPLUS

IT Disease, animal
(**mannose binding lectin**-mediated; monoclonal **antibody** against mannan binding lectin for regulating **lectin complement pathway** assocd. complement activation and treating cell or tissue injury-assocd. diseases)

L4 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 2001:276723 BIOSIS

DOCUMENT NUMBER: PREV200100276723

TITLE: Isolation and characterization of anti-rat mannose binding lectin antibodies.

AUTHOR(S): Jordan, James E. (1); Morrissey, Margaret A. (1); Stahl, Gregory L. (1)

CORPORATE SOURCE: (1) Brigham and Women's Hospital, 75 Francis St., Boston, MA, 02115 USA

SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A338. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Complement is a major participant in post-ischemic reperfusion injury. The classical and alternative complement pathways have been extensively studied; however, the role of the **lectin complement pathway** (**LCP**) in inflammation has not been investigated since inhibitors of MBL have not been described. In order to delineate the participation of the **LCP**, we generated **antibodies** to rat **mannose binding lectin** (**MBL**). In this study, **antibodies** (Ab) were produced and characterized for potential use in further dissecting the role of the **LCP** in rat models of human disease. Polyclonal and monoclonal **antibodies** were produced in rabbits and mice using purified **MBL** isolated from rat sera by affinity chromatography and standard immunization techniques. All antibodies were screened using 2 different ELISA systems (binding to mannan or BSA coupled to N-acetyl-D-glucosamine; BSA-GlcNAc) to detect complement activation and deposition of C3. Monoclonal Ab P7E4 inhibited C3 deposition onto BSA-GlcNAc coated plates in a concentration-dependent manner with maximal inhibition (apprx80%) occurring at 10 mug/mL. Similarly, Fab fragments of the polyclonal antibody inhibited complement deposition in a concentration dependent manner. Western blot analysis was performed to determine the isoform(s) of rat **MBL** that the **antibodies** recognized. While the polyclonal Ab recognized multiple oligomers of A and C isoforms under non-reducing conditions, mAb P7E4 only recognized the A isoform. Similar results were obtained under reducing conditions in that the polyclonal Ab recognized both forms while only the A isoform was recognized by P7E4. These data confirm that the **antibodies** recognize rat **mannose binding lectin**, inhibit the function of **MBL** and may serve as useful reagents in studying the **lectin complement pathway** in rat models of human disease.

AB. . . participant in post-ischemic reperfusion injury. The classical and alternative complement pathways have been extensively studied; however, the role of the **lectin complement pathway** (**LCP**) in inflammation has not been investigated since inhibitors of MBL have not been described. In order to delineate the participation of the **LCP**, we generated **antibodies** to rat **mannose binding lectin** (**MBL**). In this study, **antibodies** (Ab) were produced and characterized for potential use in further dissecting the role of the **LCP** in rat models of human disease. Polyclonal and monoclonal **antibodies** were produced in rabbits and mice using purified **MBL** isolated from rat sera by affinity chromatography and standard immunization techniques. All antibodies were screened using 2 different ELISA systems. . . antibody inhibited complement deposition in a concentration dependent manner. Western blot analysis was performed to determine the isoform(s) of rat **MBL** that the **antibodies** recognized. While the polyclonal Ab recognized multiple oligomers of A and C isoforms under non-reducing conditions, mAb P7E4 only recognized. . . the polyclonal Ab recognized both forms while only the A isoform was recognized by P7E4. These data confirm that the **antibodies** recognize rat **mannose binding lectin**, inhibit the function of **MBL** and may serve as useful reagents in studying the **lectin complement pathway** in rat models of human disease.

IT . . .
Molecular Biophysics

IT Parts, Structures, & Systems of Organisms
serum: blood and lymphatics

IT Chemicals & Biochemicals
C3: deposition; anti-rat-**mannose binding lectin antibodies**: characterization, isolation; complement: activation; **lectin complement**

pathway; mannose binding lectin

L4 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:257627 BIOSIS
DOCUMENT NUMBER: PREV200100257627
TITLE: Regulation of pro-inflammatory genes by the lectin complement pathway following myocardial ischemia-reperfusion.
AUTHOR(S): Jordan, James E. (1); Montalto, Michael C. (1); Lopes da Rosa, Jessica R. (1); Stahl, Gregory L. (1)
CORPORATE SOURCE: (1) Brigham and Women's Hospital, 75 Francis St., Boston, MA, 02115 USA
SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A463. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Reperfusion of ischemic myocardium initiates an inflammatory-like process leading to additional tissue injury. Following myocardial ischemia and reperfusion (MI/R), complement is activated with a subsequent increase in pro-inflammatory cytokines and adhesion molecule gene expression. Increasing evidence suggests that the **lectin complement pathway** (**LCP**) is involved in initiating the complement cascade following MI/R. In this study, we assessed the result of inhibiting complement activation via the **LCP** on the expression of inflammatory genes (cytokines and adhesion molecules) following MI/R. Male Sprague-Dawley rats were subjected to 30 minutes of ischemia followed by 4 hours of reperfusion. Prior to occlusion, rats were treated with 1 mg/kg P7E4 (a mAb against rat **mannose binding lectin-MBL** A) or GS-1 (an isotype control **antibody**). Following 4 hours of reperfusion, the hearts were removed, washed in saline and the area at risk was frozen in liquid nitrogen. Total RNA was isolated using the acid-guanidinium thiocyanate extraction procedure and subjected to DNAse treatment. Semi-quantitative RT-PCR was performed to assess mRNA levels of ICAM-1, TNF-alpha, iNOS, eNOS, SOD (Cu/Zn and Mn) GM-CSF and IL-1 alpha, in sham operated animals and those treated with GS-1 or P7E4 as described above. Ischemia-reperfusion resulted in the increased expression of ICAM-1*, iNOS*, TNF-alpha*, GM-CSF* and IL-alpha* compared to sham operated controls. Inhibition of MBL A attenuated the increased expression for ICAM-1*, GM-CSF*, IL-1 alpha* and iNOS. These data suggest that inhibition of MBL A and the **lectin complement pathway** results in the attenuation of inflammatory gene expression and that this gene regulation may be partially responsible for the protection from MI/R injury, * $p < 0.05$.
AB. . . complement is activated with a subsequent increase in pro-inflammatory cytokines and adhesion molecule gene expression. Increasing evidence suggests that the **lectin complement pathway** (**LCP**) is involved in initiating the complement cascade following MI/R. In this study, we assessed the result of inhibiting complement activation via the **LCP** on the expression of inflammatory genes (cytokines and adhesion molecules) following MI/R. Male Sprague-Dawley rats were subjected to 30 minutes. . . followed by 4 hours of reperfusion. Prior to occlusion, rats were treated with 1 mg/kg P7E4 (a mAb against rat **mannose binding lectin -MBL** A) or GS-1 (an isotype control **antibody**). Following 4 hours of reperfusion, the hearts were removed, washed in saline and the area at risk was frozen in. . . the increased expression for ICAM-1*, GM-CSF*, IL-1 alpha* and iNOS. These data suggest that inhibition of MBL A and the **lectin complement pathway** results in the attenuation of inflammatory gene expression and that this gene regulation may be partially responsible for the protection. . .

=> s HB-12621
L5 1 HB-12621

=> dis 15 ibib abs kwic

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:420986 CAPLUS
DOCUMENT NUMBER: 133:57580
TITLE: Methods and products for regulating lectin complement pathway associated complement activation
INVENTOR(S): Stahl, Gregory L.; Collard, Charles D.
PATENT ASSIGNEE(S): Brigham and Women's Hospital, Inc., USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035483	A1	20000622	WO 1999-US29919	19991215

W: CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: US 1998-112390 P 19981215
AB The invention relates to methods and products for regulating lectin complement pathway assocd. complement activation. The methods include both in vitro and in vivo methods for inhibiting lectin complement pathway assocd. complement activation. The methods are accomplished by contacting a mammalian cell having surface exposed MBL ligand with an effective amt. of a mannan binding lectin inhibitor to inhibit lectin complement pathway assocd. complement activation. The mannan binding lectin inhibitor may be administered to a subject to prevent cellular injury mediated by lectin complement pathway assocd. complement activation. The products of the invention include compns. of a mannan binding lectin inhibitor. The mannan binding lectin inhibitor is an isolated mannan binding lectin binding peptide that selectively binds to a human mannan binding lectin epitope and that inhibits lectin complement pathway assocd. complement activation. The products also include hybridoma cell lines and pharmaceutical compns.
REFERENCE COUNT: 4
REFERENCE(S): (1) Endo; International Immunology 1996, V8(9), P1355 CAPLUS

(2) Endo; Journal of ɔlogy 1998, V161, P4924 CAPLUS
(3) Sato; International Immunology 1994, V6(4), P665 CAPLUS
(4) Thiel; Nature 1997, V386, P506 CAPLUS

IT Hybridoma
(ATCC No. HB-12619-HB-12621; monoclonal antibody against mannan binding lectin for regulating lectin complement pathway assocd. complement activation and treating cell or tissue injury-assocd. diseases)

=> dis his

(FILE 'HOME' ENTERED AT 20:38:31 ON 17 JUL 2001)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 20:38:50 ON 17 JUL 2001
L1 0 S MBL (5N) (ANTIBOD)
L2 107 S ((MBL) OR (MANNOSE BINDING LECTIN)) (10N) (ANTIBOD?)
L3 47 DUP REM L2 (60 DUPLICATES REMOVED)
L4 6 S L3 (P) ((LCP) OR (LECTIN COMPLEMENT PATHWAY))
L5 1 S HB-12621

=> s HB-12620
L6 0 HB-12620

=> s HB-12629
L7 0 HB-12629

=> s ((MBL) or mannose binding lectin) (P) ((LCP) or lectin complement pathway)
L8 27 ((MBL) OR MANNOSE BINDING LECTIN) (P) ((LCP) OR LECTIN COMPLEMEN T PATHWAY)

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9 14 DUP REM L8 (13 DUPLICATES REMOVED)

=> dis l9 1-14 ibib abs kwic

L9 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:197043 CAPLUS
DOCUMENT NUMBER: 134:188227
TITLE: Inhibitors of the lectin complement pathway (LCP) and their use
INVENTOR(S): Stahl, Gregory L.; Lekowski, Robert
PATENT ASSIGNEE(S): The Brigham and Women's Hospital, Inc., USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012212	A1	20010222	WO 2000-US22123	20000814

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-148815 P 19990813
AB The invention relates to methods and products for regulating **lectin complement pathway** assocd. complement activation. The methods include both in vitro and in vivo methods for inhibiting **lectin complement pathway** assocd. complement activation. The methods are accomplished by contacting a mammalian cell having surface exposed **MBL** ligand with an effective amt. of a mannan binding lectin (**MBL**) receptor antagonist to inhibit **lectin complement pathway** assocd. complement activation. The mannan binding lectin receptor antagonist may be administered to a subject to prevent cellular injury mediated by **lectin complement pathway** assocd. complement activation. The products of the invention include compns. of a mannan binding lectin receptor antagonist. The mannan binding lectin receptor antagonist is an isolated mannan binding lectin that selectively binds to a human mannan binding lectin epitope and that inhibits **lectin complement pathway** assocd. complement activation.
REFERENCE COUNT: 9
REFERENCE(S): (1) Brigham & Womens Hospital; WO 0035483 A 2000 CAPLUS
(5) Holtzhauer, M; WO 9939209 A 1999 CAPLUS
(7) Lhotta, K; NEPHROLOGY, DIALYSIS, TRANSPLANTATION 1999, V14(4), P881 MEDLINE
(8) Shikhman, A; JOURNAL OF IMMUNOLOGY 1994, V153(12), P5593 CAPLUS
(9) Turner, M; IMMUNOLOGY TODAY 1996, V17(11), P532 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB The invention relates to methods and products for regulating **lectin complement pathway** assocd. complement activation. The methods include both in vitro and in vivo methods for inhibiting **lectin complement pathway** assocd. complement activation. The methods are accomplished by contacting a mammalian cell having surface exposed **MBL** ligand with an effective amt. of a mannan binding lectin (**MBL**) receptor antagonist to inhibit **lectin complement pathway** assocd. complement activation. The mannan binding lectin receptor antagonist may be administered to a subject to prevent cellular injury mediated by **lectin complement pathway** assocd. complement activation. The products of the invention include compns. of a mannan binding lectin receptor antagonist. The mannan binding lectin receptor antagonist is an isolated mannan binding lectin that selectively binds to a human mannan binding lectin epitope and that inhibits **lectin complement pathway** assocd. complement activation.
IT Keratins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(1, as mannan-binding lectin receptor; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LAA-I (Laburnum alpinum I); mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(UEA-II (Ulex europaeus II); mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Complement
(activation, lectin pathway; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Respiratory distress syndrome
(adult, inhibition of cellular injury from; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Drug delivery systems
(aerosols; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-H(O) CSA-1 (Cytisus sessilifolius 1); mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Cytisus sessilifolius
(anti-H(O) lectin 1 (CSA-1) of; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Keratins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antibodies to; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Heart, disease
(infarction, inhibition of cellular injury from; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Arthritis
Atherosclerosis
Cardiopulmonary bypass
Dialysis
Ischemia
Lupus erythematosus
Transplant and Transplantation
(inhibition of cellular injury from; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Reperfusion
Respiratory tract
(injury, inhibition of cellular injury from; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Laburnum alpinum
(lectin LAA-I of; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Ulex europaeus
(lectin UEA-II of; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(lectin, mannan-binding; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Legume (Fabaceae)
(lectins of; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(legume-derived; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Drug delivery systems
(localized; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Cytoprotective agents
Drug screening
(mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway** (**LCP**) and their use)

IT Structure-activity relationship
(mannan-binding lectin receptor antagonist of peptides; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway (LCP)** and their use)

IT Peptide library
(mannan-binding lectin receptor antagonists; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway (LCP)** and their use)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(mannan-binding lectin receptor antagonists; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway (LCP)** and their use)

IT Agglutinins and Lectins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(mannan-binding, treatment of disorders mediated by; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway (LCP)** and their use)

IT Brain, disease
(stroke, inhibition of cellular injury from; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway (LCP)** and their use)

IT Lupus erythematosus
(systemic, inhibition of cellular injury from; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway (LCP)** and their use)

IT Antibodies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to keratin; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway (LCP)** and their use)

IT 160071-01-2 160071-68-1 160071-69-2 160071-70-5 160071-71-6
160071-76-1 160071-77-2 160071-78-3 160071-79-4 160071-83-0
160071-84-1 160071-85-2 160071-86-3 160071-87-4
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(mannan-binding lectin receptor antagonist; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of **lectin complement pathway (LCP)** and their use)

L9 ANSWER 2 OF 14 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001259476 MEDLINE
DOCUMENT NUMBER: 21136395 PubMed ID: 11238665
TITLE: A keratin peptide inhibits mannose-binding lectin.
AUTHOR: Montalto M C; Collard C D; Buras J A; Reenstra W R; McClaine R; Gies D R; Rother R P; Stahl G L
CORPORATE SOURCE: Department of Anesthesiology, Perioperative and Pain Medicine, Center for Experimental Therapeutics and Reperfusion Injury, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, USA.
CONTRACT NUMBER: F32 HL-103870 (NHLBI)
HL-03854 (NHLBI)
HL-56086 (NHLBI)
SOURCE: JOURNAL OF IMMUNOLOGY, (2001 Mar 15) 166 (6) 4148-53.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered Medline: 20010517

AB Complement plays a significant role in mediating endothelial injury following oxidative stress. We have previously demonstrated that the **lectin complement pathway (LCP)**, which is initiated by deposition of the **mannose-binding lectin (MBL)**, is largely responsible for activating complement on endothelial cells following periods of oxidative stress. Identifying functional inhibitors that block **MBL** binding will be useful in characterizing the role of the **LCP** in disease models. The human cytokeratin peptide SFGSGFGGGY has been identified as a molecular mimic of N-acetyl-D-glucosamine (GlcNAc), a known ligand of **MBL**. Thus, we hypothesized that this peptide would specifically bind to **MBL** and functionally inhibit the **LCP** on endothelial cells following oxidative stress. Using a BIAcore 3000 optical biosensor, competition experiments were performed to demonstrate that the peptide SFGSGFGGGY inhibits binding of purified recombinant human **MBL** to GlcNAc in a concentration-dependent manner. Solution affinity data generated by BIAcore indicate this peptide binds to **MBL** with an affinity (K(D)) of 5 x 10(-5) mol/L. Pretreatment of human serum (30%) with the GlcNAc-mimicking peptide (10-50 microg/ml) significantly attenuated **MBL** and C3 deposition on human endothelial cells subjected to oxidative stress in a dose-dependent manner, as demonstrated by cell surface ELISA and confocal microscopy. Additionally, this decapeptide sequence attenuated complement-dependent VCAM-1 expression following oxidative stress. These data indicate that a short peptide sequence that mimics GlcNAc can specifically bind to **MBL** and functionally inhibit the proinflammatory action of the **LCP** on oxidatively stressed endothelial cells.

AB Complement plays a significant role in mediating endothelial injury following oxidative stress. We have previously demonstrated that the **lectin complement pathway (LCP)**, which is initiated by deposition of the **mannose-binding lectin (MBL)**, is largely responsible for activating complement on endothelial cells following periods of oxidative stress. Identifying functional inhibitors that block **MBL** binding will be useful in characterizing the role of the **LCP** in disease models. The human cytokeratin peptide SFGSGFGGGY has been identified as a molecular mimic of N-acetyl-D-glucosamine (GlcNAc), a known ligand of **MBL**. Thus, we hypothesized that this peptide would specifically

bind to **MBL** and functionally inhibit the [redacted] on endothelial cells following oxidative stress. Using a BIAcore 3000 optical biosensor, competition experiments were performed to demonstrate that the peptide SFGSGFGGGY inhibits binding of purified recombinant human **MBL** to GlcNAc in a concentration-dependent manner. Solution affinity data generated by BIAcore indicate this peptide binds to **MBL** with an affinity (K(D)) of 5 x 10(-5) mol/L. Pretreatment of human serum (30%) with the GlcNAc-mimicking peptide (10-50 microg/ml) significantly attenuated **MBL** and C3 deposition on human endothelial cells subjected to oxidative stress in a dose-dependent manner, as demonstrated by cell surface. . . VCAM-1 expression following oxidative stress. These data indicate that a short peptide sequence that mimics GlcNAc can specifically bind to **MBL** and functionally inhibit the proinflammatory action of the **LCP** on oxidatively stressed endothelial cells.

L9 ANSWER 3 OF 14 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:257627 BIOSIS
DOCUMENT NUMBER: PREV200100257627
TITLE: Regulation of pro-inflammatory genes by the lectin complement pathway following myocardial ischemia-reperfusion.
AUTHOR(S): Jordan, James E. (1); Montalto, Michael C. (1); Lopes da Rosa, Jessica R. (1); Stahl, Gregory L. (1)
CORPORATE SOURCE: (1) Brigham and Women's Hospital, 75 Francis St., Boston, MA, 02115 USA
SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A463. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Reperfusion of ischemic myocardium initiates an inflammatory-like process leading to additional tissue injury. Following myocardial ischemia and reperfusion (MI/R), complement is activated with a subsequent increase in pro-inflammatory cytokines and adhesion molecule gene expression. Increasing evidence suggests that the **lectin complement pathway** (**LCP**) is involved in initiating the complement cascade following MI/R. In this study, we assessed the result of inhibiting complement activation via the **LCP** on the expression of inflammatory genes (cytokines and adhesion molecules) following MI/R. Male Sprague-Dawley rats were subjected to 30 minutes of ischemia followed by 4 hours of reperfusion. Prior to occlusion, rats were treated with 1 mg/kg P7E4 (a mAb against rat **mannose binding lectin-MBL** A) or GS-1 (an isotype control antibody). Following 4 hours of reperfusion, the hearts were removed, washed in saline and the area at risk was frozen in liquid nitrogen. Total RNA was isolated using the acid-guanidinium thiocyanate extraction procedure and subjected to DNAse treatment. Semi-quantitative RT-PCR was performed to assess mRNA levels of ICAM-1, TNF-alpha, iNOS, eNOS, SOD (Cu/Zn and Mn) GM-CSF and IL-1 alpha, in sham operated animals and those treated with GS-1 or P7E4 as described above. Ischemia-reperfusion resulted in the increased expression of ICAM-1*, iNOS*, TNF-alpha*, GM-CSF* and IL-alpha* compared to sham operated controls. Inhibition of **MBL** A attenuated the increased expression for ICAM-1*, GM-CSF*, IL-1 alpha* and iNOS. These data suggest that inhibition of **MBL** A and the **lectin complement pathway** results in the attenuation of inflammatory gene expression and that this gene regulation may be partially responsible for the protection from MI/R injury, * p < 0.05.
AB. . . complement is activated with a subsequent increase in pro-inflammatory cytokines and adhesion molecule gene expression. Increasing evidence suggests that the **lectin complement pathway** (**LCP**) is involved in initiating the complement cascade following MI/R. In this study, we assessed the result of inhibiting complement activation via the **LCP** on the expression of inflammatory genes (cytokines and adhesion molecules) following MI/R. Male Sprague-Dawley rats were subjected to 30 minutes. . . followed by 4 hours of reperfusion. Prior to occlusion, rats were treated with 1 mg/kg P7E4 (a mAb against rat **mannose binding lectin -MBL** A) or GS-1 (an isotype control antibody). Following 4 hours of reperfusion, the hearts were removed, washed in saline and. . . Ischemia-reperfusion resulted in the increased expression of ICAM-1*, iNOS*, TNF-alpha*, GM-CSF* and IL-alpha* compared to sham operated controls. Inhibition of **MBL** A attenuated the increased expression for ICAM-1*, GM-CSF*, IL-1 alpha* and iNOS. These data suggest that inhibition of **MBL** A and the **lectin complement pathway** results in the attenuation of inflammatory gene expression and that this gene regulation may be partially responsible for the protection. . .

L9 ANSWER 4 OF 14 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:196301 BIOSIS
DOCUMENT NUMBER: PREV200100196301
TITLE: Inhibition of **mannose binding lectin** reduces myocardial reperfusion injury: A role for the **lectin complement pathway** in cardiovascular disease.
AUTHOR(S): Jordan, James E. (1); Stahl, Gregory L. (1)
CORPORATE SOURCE: (1) Dept. of Anesthesia, CET and RI, Brigham and Women's Hospital, Boston, MA USA
SOURCE: Journal of the American College of Cardiology, (February, 2001) Vol. 37, No. 2 Supplement A, pp. 378A. print.
Meeting Info.: 50th Annual Scientific Session of the American College of Cardiology Orlando, Florida, USA March 18-21, 2001
ISSN: 0735-1097.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
TI Inhibition of **mannose binding lectin** reduces myocardial reperfusion injury: A role for the **lectin complement pathway** in cardiovascular disease.

L9 ANSWER 5 OF 14 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:276725 BIOSIS
DOCUMENT NUMBER: PREV200100276725
TITLE: A peptide mimic of N-acetyl-D-glucosamine inhibits the lectin complement pathway following endothelial oxidative stress.

AUTHOR(S): Montalto, Michael C. (1); [redacted]llard, Charles D. (1); Buras, Jon A.; Reenstra, Wende R.; Geis, David; Rother, Russell P.; Stahl, Gregory L. (1)

CORPORATE SOURCE: (1) Brigham and Women's Hospital, 75 Francis Street, Boston, MA, 02115 USA

SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A339. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Complement plays a significant role in mediating endothelial damage following oxidative stress. We have previously demonstrated that the **lectin complement pathway (LCP)**, which is initiated by **mannose binding lectin** (**MBL**) deposition, is largely responsible for activating complement after endothelial oxidative stress. Identifying functional inhibitors of **MBL** will be useful in characterizing the role of the **LCP** following periods of oxidative stress. To date, peptide analogues specific for **MBL** have not been identified. The human cytokeratin peptide, SFGSGFGGGY, has previously been identified as a molecular mimic of N-acetyl-D-glucosamine (GlcNAc), a natural ligand of **MBL**. Thus, we hypothesized that the sequence SFGSGFGGGY would specifically bind **MBL** and functionally inhibit the **LCP** . Using a BIAcore 3000 optical biosensor, we performed competition experiments to demonstrate that the peptide SFGSGFGGGY can inhibit binding of recombinant human **MBL** to GlcNAc in a concentration dependent manner. Solution affinity data generated by BIAcore indicate this peptide binds to **MBL** with an affinity (KD) of 5 X 10-5 M. Pretreatment of human serum (30%) with the GlcNAc-mimicking peptide (10 - 50 mug/ml) significantly attenuated C3 deposition on oxidatively stressed endothelial cells in a dose dependent manner, as demonstrated by ELISA. Confocal microscopy experiments revealed that complement inhibition coincided with a decrease in **MBL** deposition. Additionally, this peptide significantly attenuated the complement-dependent expression of vascular cell adhesion molecule (VCAM)-1 as shown by ELISA. These data indicate that a short peptide sequence that mimics GlcNAc can specifically bind to **MBL**, with a physiologically relevant affinity, and functionally inhibit the pro-inflammatory action of the **LCP** on oxidatively stressed endothelial cells. Further, this is the first report to demonstrate that **MBL** is capable of specifically binding a non-carbohydrate ligand.

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IT . . .
Biophysics

IT Parts, Structures, & Systems of Organisms
endothelial cells

IT Chemicals & Biochemicals
C3: deposition; N-acetyl-D-glucosamine; N-acetyl-D-glucosamine peptide mimic; **lectin complement pathway**; recombinant human **mannose binding lectin**; vascular cell adhesion molecule-1

L9 ANSWER 6 OF 14 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 2001209693 MEDLINE

DOCUMENT NUMBER: 21195380 PubMed ID: 11298833

TITLE: Isolation, cloning and functional characterization of porcine mannose-binding lectin.

AUTHOR: Agah A; Montalto M C; Young K; Stahl G L

CORPORATE SOURCE: Center for Experimental Therapeutics and Reperfusion Injury, Department of Anesthesiology, Perioperative and Pain Medicine, Brigham & Women's Hospital, Harvard Medical School, Boston, MA 02115, USA.

CONTRACT NUMBER: HL52886 (NHLBI)

SOURCE: IMMUNOLOGY, (2001 Mar) 102 (3) 338-43.
Journal code: GH7; 0374672. ISSN: 0019-2805.

PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200105

ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010510

AB Binding of **mannose-binding lectin** (**MBL**), a C-type lectin, and its associated serine proteases, MASP-1 and MASP-2, to cell surface carbohydrates activates the **lectin complement pathway**. As **MBL** plays an important role in innate immunity, it has been cloned and characterized in several species. While the pig may be used as a source of organs/tissues for xenotransplantation, little is known about its **MBL**, thus, we report the isolation of three monomeric forms of **MBL** from

porcine serum. Sodium dodecyl sulphate-polyacrylamide gel electrophoresis and Coomassie staining of reduced porcine **MBL** revealed the presence of three monomeric forms with approximate molecular masses of 30 000, 32 000 and 34 000. Protein sequencing identified these monomeric forms as one single protein, suggesting post-translational modification. Western blot analysis demonstrated the cross-reactivity of anti-human **MBL** polyclonal antibody with porcine **MBL**. A full-length porcine liver **MBL** cDNA was isolated and the predicted amino acid sequence exhibited 64.9% identity with human **MBL** and 50.2% and 56.7% identity with rat A and C **MBL**, respectively. Furthermore, Northern blot analysis demonstrated the presence of a single (approximately 1.4-1.6 kilobase pair) transcript in porcine liver. Addition of purified porcine **MBL** to **MBL**-deficient human sera augmented N-acetylglucosamine inhibitable C3 deposition to mannan-coated plates in a dose-dependent manner. Taken together, these data demonstrate that porcine and human **MBL** are highly conserved, sharing structural and functional characteristics.

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L9 ANSWER 7 OF 14 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:276723 BIOSIS
DOCUMENT NUMBER: PREV200100276723
TITLE: Isolation and characterization of anti-rat mannose binding lectin antibodies.
AUTHOR(S): Jordan, James E. (1); Morrissey, Margaret A. (1); Stahl, Gregory L. (1)
CORPORATE SOURCE: (1) Brigham and Women's Hospital, 75 Francis St., Boston, MA, 02115 USA
SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A338. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Complement is a major participant in post-ischemic reperfusion injury. The classical and alternative complement pathways have been extensively studied; however, the role of the **lectin complement pathway** (**LCP**) in inflammation has not been investigated since inhibitors of **MBL** have not been described. In order to delineate the participation of the **LCP**, we generated antibodies to rat **mannose binding lectin** (**MBL**). In this study, antibodies (Ab) were produced and characterized for potential use in further dissecting the role of the **LCP** in rat models of human disease. Polyclonal and monoclonal antibodies were produced in rabbits and mice using purified **MBL** isolated from rat sera by affinity chromatography and standard immunization techniques. All antibodies were screened using 2 different ELISA systems (binding to mannan or BSA coupled to N-acetyl-D-glucosamine; BSA-GlcNAc) to detect complement activation and deposition of C3. Monoclonal Ab P7E4 inhibited C3 deposition onto BSA-GlcNAc coated plates in a concentration-dependent manner with maximal inhibition (apprx80%) occurring at 10 mug/mL. Similarly, Fab fragments of the polyclonal antibody inhibited complement deposition in a concentration dependent manner. Western blot analysis was performed to determine the isoform(s) of rat **MBL** that the antibodies recognized. While the polyclonal Ab recognized multiple oligomers of A and C isoforms under non-reducing conditions, mAb P7E4 only recognized the A isoform. Similar results were obtained under reducing conditions in that the polyclonal Ab recognized both forms while only the A isoform was recognized by P7E4. These data confirm that the antibodies recognize rat **mannose binding lectin**, inhibit the function of **MBL** and may serve as useful reagents in studying the **lectin complement pathway** in rat models of human disease.

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IT . . .
Molecular Biophysics
IT Parts, Structures, & Systems of Organisms
serum: blood and lymphatics
IT Chemicals & Biochemicals
C3: deposition; anti-rat **mannose binding lectin** antibodies: characterization, isolation; complement: activation; **lectin complement pathway**; **mannose binding lectin**

L9 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 3
ACCESSION NUMBER: 2001:456188 CAPLUS
TITLE: Ulex europaeus agglutinin II (UEA-II) is a novel, potent inhibitor of complement activation
AUTHOR(S): Lekowski, Robert; Collard, Charles D.; Reenstra, Wende R.; Stahl, Gregory L.
CORPORATE SOURCE: Center for Experimental Therapeutics and Reperfusion Injury, Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Protein Sci. (2001), 10(2), 277-284
CODEN: PRCIEI; ISSN: 0961-8368
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Complement is an important mediator of vascular injury following oxidative stress. We recently demonstrated that complement activation following endothelial oxidative stress is mediated by **mannose-binding lectin** (**MBL**) and activation of the **lectin complement pathway**. Here, we investigated whether nine plant lectins which have a binding profile similar to that of **MBL** competitively inhibit **MBL** deposition and subsequent complement activation following human umbilical vein endothelial cell (HUVEC) oxidative stress. HUVEC oxidative stress (1% O2, 24 h) significantly increased Ulex europaeus agglutinin II (UEA-II) binding by 72.+-.9% compared to normoxic cells. UEA-II inhibited **MBL** binding to HUVEC in a concn.-dependent manner following oxidative stress. Further, **MBL** inhibited UEA-II binding to HUVEC in a concn.-dependent manner following oxidative stress, suggesting a common ligand. UEA-II (.ltoreq. 100 .mu.mol/L) did not attenuate the hemolytic activity, nor did it inhibit C3a des Arg formation from alternative or classical complement pathway-specific hemolytic assays. C3 deposition (measured by ELISA) following HUVEC oxidative stress was inhibited by UEA-II in a concn.-dependent manner (IC50 = 10 pmol/L). UEA-II inhibited C3 and **MBL** co-localization (confocal microscopy) in a concn.-dependent manner on HUVEC following oxidative stress (IC50 .apprxeq. 1 pmol/L). Finally, UEA-II significantly inhibited complement-dependent neutrophil chemotaxis, but failed to inhibit fMLP-mediated chemotaxis, following endothelial oxidative stress. These data demonstrate that UEA-II is a novel, potent inhibitor of human **MBL** deposition and complement activation following human endothelial oxidative stress.
REFERENCE COUNT: 29
REFERENCE(S): (1) Alencar, N; Mediators Inflamm 1999, V8, P107 CAPLUS
(2) Bless, N; Am J Physiol 1999, V276, PL57 CAPLUS
(3) Buerke, M; Journal of Pharmacology and Experimental Therapeutics 1998, V286, P429 CAPLUS
(4) Collard, C; Am J Pathol 2000, V156, P1549 CAPLUS
(5) Collard, C; Arterioscler Thromb Vasc Biol 1999, V19, P2623 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Complement is an important mediator of vascular injury following oxidative stress. We recently demonstrated that complement activation following endothelial oxidative stress is mediated by **mannose-binding lectin** (**MBL**) and activation of the **lectin complement pathway**. Here, we investigated whether nine plant lectins which have a binding profile similar to that of **MBL** competitively inhibit **MBL** deposition and subsequent complement activation following human umbilical vein endothelial cell (HUVEC) oxidative stress. HUVEC oxidative stress (1% O2, 24 h) significantly increased Ulex europaeus agglutinin II (UEA-II) binding by 72.+-.9% compared to normoxic cells. UEA-II inhibited **MBL** binding to HUVEC in a concn.-dependent manner following oxidative stress. Further, **MBL** inhibited UEA-II binding to HUVEC in a concn.-dependent manner following oxidative stress, suggesting a common ligand. UEA-II (.ltoreq. 100 .mu.mol/L) did not attenuate the hemolytic activity, nor did it inhibit C3a des Arg formation from alternative or classical complement pathway-specific hemolytic assays. C3 deposition (measured by ELISA) following HUVEC oxidative stress was inhibited by UEA-II in a concn.-dependent manner (IC50 = 10 pmol/L). UEA-II inhibited C3 and **MBL** co-localization (confocal microscopy) in a concn.-dependent manner on HUVEC following oxidative stress (IC50 .apprxeq. 1 pmol/L). Finally, UEA-II significantly inhibited complement-dependent neutrophil chemotaxis, but failed to inhibit fMLP-mediated chemotaxis, following endothelial oxidative stress. These data demonstrate that UEA-II is a novel, potent inhibitor of human **MBL** deposition and complement activation following human endothelial oxidative stress.

L9 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:420986 CAPLUS
DOCUMENT NUMBER: 133:57580
TITLE: Methods and products for regulating lectin complement pathway associated complement activation
INVENTOR(S): Stahl, Gregory L.; Collard, Charles D.
PATENT ASSIGNEE(S): Brigham and Women's Hospital, Inc., USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035483	A1	20000622	WO 1999-US29919	19991215

W: CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1998-112390 P 19981215
AB The invention relates to methods and products for regulating **lectin complement pathway** assocd. complement

activation. The methods include both in vitro and in vivo methods for inhibiting **lectin complement pathway** assocd. complement activation. The methods are accomplished by contacting a mammalian cell having surface exposed **MBL** ligand with an effective amt. of a mannan binding lectin inhibitor to inhibit **lectin complement pathway** assocd. complement activation. The mannan binding lectin inhibitor may be administered to a subject to prevent cellular injury mediated by **lectin complement pathway** assocd. complement activation. The products of the invention include compns. of a mannan binding lectin inhibitor. The mannan binding lectin inhibitor is an isolated mannan binding lectin binding peptide that selectively binds to a human mannan binding lectin epitope and that inhibits **lectin complement pathway** assocd. complement activation. The products also include hybridoma cell lines and pharmaceutical compns.

REFERENCE COUNT: 4

REFERENCE(S):
(1) Endo; International Immunology 1996, V8(9), P1355 CAPLUS
(2) Endo; Journal of Immunology 1998, V161, P4924 CAPLUS
(3) Sato; International Immunology 1994, V6(4), P665 CAPLUS
(4) Thiel; Nature 1997, V386, P506 CAPLUS

AB The invention relates to methods and products for regulating **lectin complement pathway** assocd. complement activation. The methods include both in vitro and in vivo methods for inhibiting **lectin complement pathway** assocd. complement activation. The methods are accomplished by contacting a mammalian cell having surface exposed **MBL** ligand with an effective amt. of a mannan binding lectin inhibitor to inhibit **lectin complement pathway** assocd. complement activation. The mannan binding lectin inhibitor may be administered to a subject to prevent cellular injury mediated by **lectin complement pathway** assocd. complement activation. The products of the invention include compns. of a mannan binding lectin inhibitor. The mannan binding lectin inhibitor is an isolated mannan binding lectin binding peptide that selectively binds to a human mannan binding lectin epitope and that inhibits **lectin complement pathway** assocd. complement activation. The products also include hybridoma cell lines and pharmaceutical compns.

IT Disease, animal
(**mannose binding lectin**-mediated; monoclonal antibody against mannan binding lectin for regulating **lectin complement pathway** assocd. complement activation and treating cell or tissue injury-assocd. diseases)

L9 ANSWER 10 OF 14 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000255148 MEDLINE
DOCUMENT NUMBER: 20255148 PubMed ID: 10793066
TITLE: Complement activation after oxidative stress: role of the lectin complement pathway.
AUTHOR: Collard C D; Vakeva A; Morrissey M A; Agah A; Rollins S A; Reenstra W R; Buras J A; Meri S; Stahl G L
CORPORATE SOURCE: Center for Experimental Therapeutics and Reperfusion Injury, Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA.
CONTRACT NUMBER: HL-03854 (NHLBI)
HL-52886 (NHLBI)
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (2000 May) 156 (5) 1549-56. Journal code: 3RS; 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000616
Last Updated on STN: 20000616
Entered Medline: 20000602

AB The complement system plays an important role in mediating tissue injury after oxidative stress. The role of **mannose-binding lectin** (**MBL**) and the **lectin complement pathway** (**LCP**) in mediating complement activation after endothelial oxidative stress was investigated. iC3b deposition on hypoxic (24 hours; 1% O(2))/reoxygenated (3 hours; 21% O(2)) human endothelial cells was attenuated by N-acetyl-D-glucosamine or D-mannose, but not L-mannose, in a dose-dependent manner. Endothelial iC3b deposition after oxidative stress was also attenuated in **MBL**-deficient serum. Novel, functionally inhibitory, anti-human **MBL** monoclonal antibodies attenuated **MBL**-dependent C3 deposition on mannan-coated plates in a dose-dependent manner. Treatment of human serum with anti-**MBL** monoclonal antibodies inhibited **MBL** and C3 deposition after endothelial oxidative stress. Consistent with our in vitro findings, C3 and **MBL** immunostaining throughout the ischemic area at risk increased during rat myocardial reperfusion in vivo. These data suggest that the **LCP** mediates complement activation after tissue oxidative stress. Inhibition of **MBL** may represent a novel therapeutic strategy for ischemia/reperfusion injury and other complement-mediated disease states.

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L9 ANSWER 11 OF 14 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999262288 MEDLINE
DOCUMENT NUMBER: 99262288 PubMed ID: 10330290

TITLE: A truncated form of mannose-binding lectin-associated serine protease (MASP)-2 expressed by alternative polyadenylation is a component of the lectin complement pathway

AUTHOR: Takahashi M; Endo Y; Fujita T; Matsushita M
CORPORATE SOURCE: Department of Biochemistry, Fukushima Medical University School of Medicine, 1 Hikarigaoka, Fukushima 960-1295, Japan.
SOURCE: INTERNATIONAL IMMUNOLOGY, (1999 May) 11 (5) 859-63. Journal code: AY5; 8916182. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AB008047
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990712
Last Updated on STN: 20000303
Entered Medline: 19990623

AB The lectin complement pathway is initiated by binding of mannose-binding lectin (MBL) and MBL-associated serine protease (MASP) to carbohydrates. In the human lectin pathway, MASP-1 and MASP-2 are involved in the proteolysis of C4, C2 and C3. Here we report that the human MBL-MASP complex contains a new 22 kDa protein [small MBL -associated protein (sMAP)] bound to MASP-1. Analysis of the nucleotide sequence of sMAP cDNA revealed that it is a truncated form of MASP-2, consisting of the first two domains (i.e. the first internal repeat and the epidermal growth factor-like domain) with four different C-terminal amino acids. sMAP mRNAs are expressed in liver by alternative polyadenylation of the MASP-2 gene, in which a sMAP-specific exon containing an in-frame stop codon and a polyadenylation signal is used. The involvement of sMAP in the MBL-MASP complex suggests that the activation mechanism of the lectin pathway is more complicated than that of the classical pathway.

TI A truncated form of mannose-binding lectin -associated serine protease (MASP)-2 expressed by alternative polyadenylation is a component of the lectin complement pathway.

AB The lectin complement pathway is initiated by binding of mannose-binding lectin (MBL) and MBL-associated serine protease (MASP) to carbohydrates. In the human lectin pathway, MASP-1 and MASP-2 are involved in the proteolysis of C4, C2 and C3. Here we report that the human MBL-MASP complex contains a new 22 kDa protein [small MBL -associated protein (sMAP)] bound to MASP-1. Analysis of the nucleotide sequence of sMAP cDNA revealed that it is a truncated form. . . a sMAP-specific exon containing an in-frame stop codon and a polyadenylation signal is used. The involvement of sMAP in the MBL-MASP complex suggests that the activation mechanism of the lectin pathway is more complicated than that of the classical pathway.

L9 ANSWER 12 OF 14 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:384292 BIOSIS
DOCUMENT NUMBER: PREV199900384292
TITLE: Mannose-binding lectin co-localizes with complement in atherosclerotic human coronary arteries: A novel role for the lectin complement pathway in human cardiovascular disease.
AUTHOR(S): Vakeva, A. (1); Collard, C. D.; Laine, P.; Morse, D. S.; Paavonen, T.; Meri, S. (1); Kovanen, P. T.; Stahl, G. L.
CORPORATE SOURCE: (1) Haartman Institute, Department of Bacteriology and Immunology, University of Helsinki, Helsinki Finland
SOURCE: Molecular Immunology, (March-April, 1999) Vol. 36, No. 4-5, pp. 302.
Meeting Info.: 7th European Meeting on Complement in Human Disease Helsinki, Finland June 17-20, 1999
ISSN: 0161-5890.
DOCUMENT TYPE: Conference
LANGUAGE: English

TI Mannose-binding lectin co-localizes with complement in atherosclerotic human coronary arteries: A novel role for the lectin complement pathway in human cardiovascular disease.

L9 ANSWER 13 OF 14 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:395748 BIOSIS
DOCUMENT NUMBER: PREV199900395748
TITLE: Endothelial reoxygenation activates the lectin complement pathway: Inhibition with anti-human mannose binding lectin (MBL) therapy.
AUTHOR(S): Collard, C. D. (1); Agah, A. (1); Buras, J. A. (1); Reenstra, W. R. (1); Morrissey, M. M. (1); Stahl, G. L. (1)
CORPORATE SOURCE: (1) Center for Experimental Therapeutics and Reperfusion Injury, Dept. of Anesthesiology, Pain and Perioperative Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA USA
SOURCE: Molecular Immunology, (March April, 1999) Vol. 36, No. 4-5, pp. 278.
Meeting Info.: 7th European Meeting on Complement in Human Disease Helsinki, Finland June 17-20, 1999
ISSN: 0161-5890.
DOCUMENT TYPE: Conference
LANGUAGE: English

TI Endothelial reoxygenation activates the lectin complement pathway: Inhibition with anti-human mannose binding lectin (MBL) therapy.

L9 ANSWER 14 OF 14 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:521701 BIOSIS
DOCUMENT NUMBER: PREV199800521701
TITLE: MBL-MASP complex is associated with a truncated protein derived from MASP-2 gene by alternative RNA processing.
AUTHOR(S): Takahashi, M.; Matsushita, M.; Endo, Y.; Fujita, T.
CORPORATE SOURCE: Dep. Biochemistry, Fukushima Med. Univ. Sch. Med., 1-Hikariagoka, Fukushima Japan
SOURCE: Molecular Immunology, (April-May, 1998) Vol. 35, No. 6-7, pp. 349.
Meeting Info.: XVII International Complement Workshop

Rhodes, Greece October 11-[illegible], 1998
ISSN: 0161-5890.
DOCUMENT TYPE: Conference
LANGUAGE: English
IT Major Concepts
Biochemistry and Molecular Biophysics; Immune System (Chemical Coordination and Homeostasis)
IT Chemicals & Biochemicals
cDNA [complementary DNA]; **lectin complement pathway**: activation; **mannose binding lectin-associated serine protease**; **mannose-binding lectin**; truncated protein; RNA: alternative processing

=> dis his

(FILE 'HOME' ENTERED AT 20:38:31 ON 17 JUL 2001)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 20:38:50 ON 17 JUL 2001
L1 0 S MBL (5N) (ANTIBOD)
L2 107 S ((MBL) OR (MANNOSE BINDING LECTIN)) (10N) (ANTIBOD?)
L3 47 DUP REM L2 (60 DUPLICATES REMOVED)
L4 6 S L3 (P) ((LCP) OR (LECTIN COMPLEMENT PATHWAY))
L5 1 S HB-12621
L6 0 S HB-12620
L7 0 S HB-12629
L8 27 S ((MBL) OR MANNOSE BINDING LECTIN) (P) ((LCP) OR LECTIN COMPLE
L9 14 DUP REM L8 (13 DUPLICATES REMOVED)

=> s ((MBL) or mannose binding lectin) (P) ((LCP) or lectin complement pathway) (P) inhibit?
L10 21 ((MBL) OR MANNOSE BINDING LECTIN) (P) ((LCP) OR LECTIN COMPLEMEN
T PATHWAY) (P) INHIBIT?

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11 11 DUP REM L10 (10 DUPLICATES REMOVED)

=> dis l11 1-11 ibib abs kwic

L11 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:137043 CAPLUS
DOCUMENT NUMBER: 134:188227
TITLE: Inhibitors of the lectin complement pathway (LCP) and their use
INVENTOR(S): Stahl, Gregory L.; Lekowski, Robert
PATENT ASSIGNEE(S): The Brigham and Women's Hospital, Inc., USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012212	A1	20010222	WO 2000-US22123	20000814

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-148815 P 19990813
AB The invention relates to methods and products for regulating **lectin complement pathway** assocd. complement activation. The methods include both in vitro and in vivo methods for **inhibiting lectin complement pathway** assocd. complement activation. The methods are accomplished by contacting a mammalian cell having surface exposed **MBL** ligand with an effective amt. of a mannan binding lectin (**MBL**) receptor antagonist to **inhibit lectin complement pathway** assocd. complement activation. The mannan binding lectin receptor antagonist may be administered to a subject to prevent cellular injury mediated by **lectin complement pathway** assocd. complement activation. The products of the invention include compns. of a mannan binding lectin receptor antagonist. The mannan binding lectin receptor antagonist is an isolated mannan binding lectin that selectively binds to a human mannan binding lectin epitope and that **inhibits lectin complement pathway** assocd. complement activation.
REFERENCE COUNT: 9
REFERENCE(S):
(1) Brigham & Womens Hospital; WO 0035483 A 2000 CAPLUS
(5) Holtzhauer, M; WO 9939209 A 1999 CAPLUS
(7) Lhotta, K; NEPHROLOGY, DIALYSIS, TRANSPLANTATION 1999, V14(4), P881 MEDLINE
(8) Shikhman, A; JOURNAL OF IMMUNOLOGY 1994, V153(12), P5593 CAPLUS
(9) Turner, M; IMMUNOLOGY TODAY 1996, V17(11), P532 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The invention relates to methods and products for regulating **lectin complement pathway** assocd. complement activation. The methods include both in vitro and in vivo methods for **inhibiting lectin complement pathway** assocd. complement activation. The methods are accomplished by contacting a mammalian cell having surface exposed **MBL** ligand with an effective amt. of a mannan binding lectin (**MBL**) receptor antagonist to **inhibit lectin complement pathway** assocd. complement activation. The mannan binding lectin receptor antagonist may be administered to a subject to prevent cellular injury mediated by **lectin complement pathway** assocd. complement activation. The products of the invention include compns. of a mannan binding lectin receptor antagonist. The mannan binding lectin receptor antagonist is an isolated mannan binding lectin that selectively binds to a human mannan binding lectin epitope and that **inhibits lectin complement pathway** assocd. complement activation.
IT Keratins

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(1, as mannan-binding lectin receptor; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LAA-I (Laburnum alpinum I); mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(UEA-II (Ulex europaeus II); mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Complement
(activation, lectin pathway; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Respiratory distress syndrome
(adult, inhibition of cellular injury from; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Drug delivery systems
(aerosols; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-H(O) CSA-1 (Cytisus sessilifolius 1); mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Cytisus sessilifolius
(anti-H(O) lectin 1 (CSA-1) of; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Keratins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antibodies to; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Heart, disease
(infarction, inhibition of cellular injury from; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Arthritis
Atherosclerosis
Cardiopulmonary bypass
Dialysis
Ischemia
Lupus erythematosus
Transplant and Transplantation
(inhibition of cellular injury from; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Reperfusion
Respiratory tract
(injury, inhibition of cellular injury from; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Laburnum alpinum
(lectin LAA-I of; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Ulex europaeus
(lectin UEA-II of; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(lectin, mannan-binding; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Legume (Fabaceae)
(lectins of; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Agglutinins and Lectins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(legume-derived; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Drug delivery systems
(localized; mannan binding lectin (MBL) receptor antagonists such as legume-derived lectin or anti-keratin antibody as inhibitors of lectin complement pathway (LCP) and their use)

IT Cytoprotective agents
Drug screening

(mannan binding lectin (MBL) recepto agonists such as legume-derived lectin or anti-keratin antibody as **inhibitors** of **lectin complement pathway** (**LCP**) and their use)

IT Structure-activity relationship
(mannan-binding lectin receptor antagonist of peptides; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as **inhibitors** of **lectin complement pathway** (**LCP**) and their use)

IT Peptide library
(mannan-binding lectin receptor antagonists; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as **inhibitors** of **lectin complement pathway** (**LCP**) and their use)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(mannan-binding lectin receptor antagonists; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as **inhibitors** of **lectin complement pathway** (**LCP**) and their use)

IT Agglutinins and Lectins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(mannan-binding, treatment of disorders mediated by; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as **inhibitors** of **lectin complement pathway** (**LCP**) and their use)

IT Brain, disease
(stroke, **inhibition** of cellular injury from; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as **inhibitors** of **lectin complement pathway** (**LCP**) and their use)

IT Lupus erythematosus
(systemic, **inhibition** of cellular injury from; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as **inhibitors** of **lectin complement pathway** (**LCP**) and their use)

IT Antibodies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biplogical study); USES (Uses)
(to keratin; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as **inhibitors** of **lectin complement pathway** (**LCP**) and their use)

IT 160071-01-2 160071-68-1 160071-69-2 160071-70-5 160071-71-6
160071-76-1 160071-77-2 160071-78-3 160071-79-4 160071-83-0
160071-84-1 160071-85-2 160071-86-3 160071-87-4
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(mannan-binding lectin receptor antagonist; mannan binding lectin (**MBL**) receptor antagonists such as legume-derived lectin or anti-keratin antibody as **inhibitors** of **lectin complement pathway** (**LCP**) and their use)

L11 ANSWER 2 OF 11 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001259476 MEDLINE
DOCUMENT NUMBER: 21136395 PubMed ID: 11238665
TITLE: A keratin peptide inhibits mannose-binding lectin.
AUTHOR: Montalto M C; Collard C D; Buras J A; Reenstra W R; McClaine R; Gies D R; Rother R P; Stahl G L
CORPORATE SOURCE: Department of Anesthesiology, Perioperative and Pain Medicine, Center for Experimental Therapeutics and Reperfusion Injury, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, USA.
CONTRACT NUMBER: F32 HL-103870 (NHLBI)
HL-03854 (NHLBI)
HL-56086 (NHLBI)
SOURCE: JOURNAL OF IMMUNOLOGY, (2001 Mar 15) 166 (6) 4148-53.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered Medline: 20010517

AB Complement plays a significant role in mediating endothelial injury following oxidative stress. We have previously demonstrated that the **lectin complement pathway** (**LCP**), which is initiated by deposition of the **mannose-binding lectin** (**MBL**), is largely responsible for activating complement on endothelial cells following periods of oxidative stress. Identifying functional **inhibitors** that block **MBL** binding will be useful in characterizing the role of the **LCP** in disease models. The human cytokeratin peptide SFGSGFGGGY has been identified as a molecular mimic of N-acetyl-D-glucosamine (GlcNAc), a known ligand of **MBL**. Thus, we hypothesized that this peptide would specifically bind to **MBL** and functionally **inhibit** the **LCP** on endothelial cells following oxidative stress. Using a BIAcore 3000 optical biosensor, competition experiments were performed to demonstrate that the peptide SFGSGFGGGY **inhibits** binding of purified recombinant human **MBL** to GlcNAc in a concentration-dependent manner. Solution affinity data generated by BIAcore indicate this peptide binds to **MBL** with an affinity (K(D)) of 5 x 10(-5) mol/L. Pretreatment of human serum (30%) with the GlcNAc-mimicking peptide (10-50 microg/ml) significantly attenuated **MBL** and C3 deposition on human endothelial cells subjected to oxidative stress in a dose-dependent manner, as demonstrated by cell surface ELISA and confocal microscopy. Additionally, this decapeptide sequence attenuated complement-dependent VCAM-1 expression following oxidative stress. These data indicate that a short peptide sequence that mimics GlcNAc can specifically bind to **MBL** and functionally **inhibit** the proinflammatory action of the **LCP** on oxidatively stressed endothelial cells.

AB Complement plays a significant role in mediating endothelial injury following oxidative stress. We have previously demonstrated that the

lectin complement pathway (LCP), which is initiated by deposition of the mannose-binding lectin (MBL), is largely responsible for activating complement on endothelial cells following periods of oxidative stress. Identifying functional inhibitors that block MBL binding will be useful in characterizing the role of the LCP in disease models. The human cytokeratin peptide SFGSGFGGGY has been identified as a molecular mimic of N-acetyl-D-glucosamine (GlcNAc), a known ligand of MBL. Thus, we hypothesized that this peptide would specifically bind to MBL and functionally inhibit the LCP on endothelial cells following oxidative stress. Using a BIAcore 3000 optical biosensor, competition experiments were performed to demonstrate that the peptide SFGSGFGGGY inhibits binding of purified recombinant human MBL to GlcNAc in a concentration-dependent manner. Solution affinity data generated by BIAcore indicate this peptide binds to MBL with an affinity (K(D)) of 5 x 10(-5) mol/L. Pretreatment of human serum (30%) with the GlcNAc-mimicking peptide (10-50 microg/ml) significantly attenuated MBL and C3 deposition on human endothelial cells subjected to oxidative stress in a dose-dependent manner, as demonstrated by cell surface. . . VCAM-1 expression following oxidative stress. These data indicate that a short peptide sequence that mimics GlcNAc can specifically bind to MBL and functionally inhibit the proinflammatory action of the LCP on oxidatively stressed endothelial cells.

L11 ANSWER 3 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:257627 BIOSIS
DOCUMENT NUMBER: PREV200100257627
TITLE: Regulation of pro-inflammatory genes by the lectin complement pathway following myocardial ischemia-reperfusion.
AUTHOR(S): Jordan, James E. (1); Montalto, Michael C. (1); Lopes da Rosa, Jessica R. (1); Stahl, Gregory L. (1)
CORPORATE SOURCE: (1) Brigham and Women's Hospital, 75 Francis St., Boston, MA, 02115 USA
SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A463. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Reperfusion of ischemic myocardium initiates an inflammatory-like process leading to additional tissue injury. Following myocardial ischemia and reperfusion (MI/R), complement is activated with a subsequent increase in pro-inflammatory cytokines and adhesion molecule gene expression. Increasing evidence suggests that the lectin complement pathway (LCP) is involved in initiating the complement cascade following MI/R. In this study, we assessed the result of inhibiting complement activation via the LCP on the expression of inflammatory genes (cytokines and adhesion molecules) following MI/R. Male Sprague-Dawley rats were subjected to 30 minutes of ischemia followed by 4 hours of reperfusion. Prior to occlusion, rats were treated with 1 mg/kg P7E4 (a mAb against rat mannose binding lectin-MBL A) or GS-1 (an isotype control antibody). Following 4 hours of reperfusion, the hearts were removed, washed in saline and the area at risk was frozen in liquid nitrogen. Total RNA was isolated using the acid-guanidinium thiocyanate extraction procedure and subjected to DNAse treatment. Semi-quantitative RT-PCR was performed to assess mRNA levels of ICAM-1, TNF-alpha, iNOS, eNOS, SOD (Cu/Zn and Mn) GM-CSF and IL-1 alpha, in sham operated animals and those treated with GS-1 or P7E4 as described above. Ischemia-reperfusion resulted in the increased expression of ICAM-1*, iNOS*, TNF-alpha*, GM-CSF* and IL-alpha* compared to sham operated controls. Inhibition of MBL A attenuated the increased expression for ICAM-1*, GM-CSF*, IL-1 alpha* and iNOS. These data suggest that inhibition of MBL A and the lectin complement pathway results in the attenuation of inflammatory gene expression and that this gene regulation may be partially responsible for the protection from MI/R injury, * p < 0.05.
AB. . . complement is activated with a subsequent increase in pro-inflammatory cytokines and adhesion molecule gene expression. Increasing evidence suggests that the lectin complement pathway (LCP) is involved in initiating the complement cascade following MI/R. In this study, we assessed the result of inhibiting complement activation via the LCP on the expression of inflammatory genes (cytokines and adhesion molecules) following MI/R. Male Sprague-Dawley rats were subjected to 30 minutes. . . followed by 4 hours of reperfusion. Prior to occlusion, rats were treated with 1 mg/kg P7E4 (a mAb against rat mannose binding lectin-MBL A) or GS-1 (an isotype control antibody). Following 4 hours of reperfusion, the hearts were removed, washed in saline and. . . described above. Ischemia-reperfusion resulted in the increased expression of ICAM-1*, iNOS*, TNF-alpha*, GM-CSF* and IL-alpha* compared to sham operated controls. Inhibition of MBL A attenuated the increased expression for ICAM-1*, GM-CSF*, IL-1 alpha* and iNOS. These data suggest that inhibition of MBL A and the lectin complement pathway results in the attenuation of inflammatory gene expression and that this gene regulation may be partially responsible for the protection. . .

L11 ANSWER 4 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:196301 BIOSIS
DOCUMENT NUMBER: PREV200100196301
TITLE: Inhibition of mannose binding lectin reduces myocardial reperfusion injury: A role for the lectin complement pathway in cardiovascular disease.
AUTHOR(S): Jordan, James E. (1); Stahl, Gregory L. (1)
CORPORATE SOURCE: (1) Dept. of Anesthesia, CET and RI, Brigham and Women's Hospital, Boston, MA USA
SOURCE: Journal of the American College of Cardiology, (February, 2001) Vol. 37, No. 2 Supplement A, pp. 378A. print.
Meeting Info.: 50th Annual Scientific Session of the American College of Cardiology Orlando, Florida, USA March 18-21, 2001
ISSN: 0735-1097.
DOCUMENT TYPE: Conference
LANGUAGE: English

SUMMARY LANGUAGE: English
TI **Inhibition of mannose binding lectin** reduces myocardial reperfusion injury: A role for the **lectin complement pathway** in cardiovascular disease.

L11 ANSWER 5 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:276725 BIOSIS
DOCUMENT NUMBER: PREV200100276725
TITLE: A peptide mimic of N-acetyl-D-glucosamine inhibits the lectin complement pathway following endothelial oxidative stress.
AUTHOR(S): Montalto, Michael C. (1); Collard, Charles D. (1); Buras, Jon A.; Reenstra, Wende R.; Geis, David; Rother, Russell P.; Stahl, Gregory L. (1)
CORPORATE SOURCE: (1) Brigham and Women's Hospital, 75 Francis Street, Boston, MA, 02115 USA
SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A339. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Complement plays a significant role in mediating endothelial damage following oxidative stress. We have previously demonstrated that the **lectin complement pathway (LCP)**, which is initiated by **mannose binding lectin** (**MBL**) deposition, is largely responsible for activating complement after endothelial oxidative stress. Identifying functional **inhibitors** of **MBL** will be useful in characterizing the role of the **LCP** following periods of oxidative stress. To date, peptide analogues specific for **MBL** have not been identified. The human cytokeratin peptide, SFGSGFGGGY, has previously been identified as a molecular mimic of N-acetyl-D-glucosamine (GlcNAc), a natural ligand of **MBL**. Thus, we hypothesized that the sequence SFGSGFGGGY would specifically bind **MBL** and functionally **inhibit** the **LCP**. Using a BIAcore 3000 optical biosensor, we performed competition experiments to demonstrate that the peptide SFGSGFGGGY can **inhibit** binding of recombinant human **MBL** to GlcNAc in a concentration dependent manner. Solution affinity data generated by BIAcore indicate this peptide binds to **MBL** with an affinity (KD) of 5 X 10-5 M. Pretreatment of human serum (30%) with the GlcNAc-mimicking peptide (10 - 50 mug/ml) significantly attenuated C3 deposition on oxidatively stressed endothelial cells in a dose dependent manner, as demonstrated by ELISA. Confocal microscopy experiments revealed that complement **inhibition** coincided with a decrease in **MBL** deposition. Additionally, this peptide significantly attenuated the complement-dependent expression of vascular cell adhesion molecule (VCAM)-1 as shown by ELISA. These data indicate that a short peptide sequence that mimics GlcNAc can specifically bind to **MBL**, with a physiologically relevant affinity, and functionally **inhibit** the pro-inflammatory action of the **LCP** on oxidatively stressed endothelial cells. Further, this is the first report to demonstrate that **MBL** is capable of specifically binding a non-carbohydrate ligand.
AB Complement plays a significant role in mediating endothelial damage following oxidative stress. We have previously demonstrated that the **lectin complement pathway (LCP)**, which is initiated by **mannose binding lectin** (**MBL**) deposition, is largely responsible for activating complement after endothelial oxidative stress. Identifying functional **inhibitors** of **MBL** will be useful in characterizing the role of the **LCP** following periods of oxidative stress. To date, peptide analogues specific for **MBL** have not been identified. The human cytokeratin peptide, SFGSGFGGGY, has previously been identified as a molecular mimic of N-acetyl-D-glucosamine (GlcNAc), a natural ligand of **MBL**. Thus, we hypothesized that the sequence SFGSGFGGGY would specifically bind **MBL** and functionally **inhibit** the **LCP**. Using a BIAcore 3000 optical biosensor, we performed competition experiments to demonstrate that the peptide SFGSGFGGGY can **inhibit** binding of recombinant human **MBL** to GlcNAc in a concentration dependent manner. Solution affinity data generated by BIAcore indicate this peptide binds to **MBL** with an affinity (KD) of 5 X 10-5 M. Pretreatment of human serum (30%) with the GlcNAc-mimicking peptide (10 -. . . on oxidatively stressed endothelial cells in a dose dependent manner, as demonstrated by ELISA. Confocal microscopy experiments revealed that complement **inhibition** coincided with a decrease in **MBL** deposition. Additionally, this peptide significantly attenuated the complement-dependent expression of vascular cell adhesion molecule (VCAM)-1 as shown by ELISA. These data indicate that a short peptide sequence that mimics GlcNAc can specifically bind to **MBL**, with a physiologically relevant affinity, and functionally **inhibit** the pro-inflammatory action of the **LCP** on oxidatively stressed endothelial cells. Further, this is the first report to demonstrate that **MBL** is capable of specifically binding a non-carbohydrate ligand.

L11 ANSWER 6 OF 11 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001209693 MEDLINE
DOCUMENT NUMBER: 21195380 PubMed ID: 11298833
TITLE: Isolation, cloning and functional characterization of porcine mannose-binding lectin.
AUTHOR: Agah A; Montalto M C; Young K; Stahl G L
CORPORATE SOURCE: Center for Experimental Therapeutics and Reperfusion Injury, Department of Anesthesiology, Perioperative and Pain Medicine, Brigham & Women's Hospital, Harvard Medical School, Boston, MA 02115, USA.
CONTRACT NUMBER: HL52886 (NHLBI)
SOURCE: IMMUNOLOGY, (2001 Mar) 102 (3) 338-43.
Journal code: GH7; 0374672. ISSN: 0019-2805.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010510
AB **Binding of mannose-binding lectin** (**MBL**), a C-type lectin, and its associated serine proteases, MASP-1 and MASP-2, to cell surface carbohydrates activates the **lectin complement pathway**. As **MBL** plays an important

role in innate immunity, it has been cloned and characterized in several species. While the pig may be used as a source of organs/tissues for xenotransplantation, little is known about its MBL, thus, we report the isolation of three monomeric forms of MBL from porcine serum. Sodium dodecyl sulphate-polyacrylamide gel electrophoresis and Coomassie staining of reduced porcine MBL revealed the presence of three monomeric forms with approximate molecular masses of 30 000, 32 000 and 34 000. Protein sequencing identified these monomeric forms as one single protein, suggesting post-translational modification. Western blot analysis demonstrated the cross-reactivity of anti-human MBL polyclonal antibody with porcine MBL. A full-length porcine liver MBL cDNA was isolated and the predicted amino acid sequence exhibited 64.9% identity with human MBL and 50.2% and 56.7% identity with rat A and C MBL, respectively. Furthermore, Northern blot analysis demonstrated the presence of a single (approximately 1.4-1.6 kilobase pair) transcript in porcine liver. Addition of purified porcine MBL to MBL-deficient human sera augmented N-acetylglucosamine inhibitable C3 deposition to mannan-coated plates in a dose-dependent manner. Taken together, these data demonstrate that porcine and human MBL are highly conserved, sharing structural and functional characteristics.

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L11 ANSWER 7 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:276723 BIOSIS
DOCUMENT NUMBER: PREV200100276723
TITLE: Isolation and characterization of anti-rat mannose binding lectin antibodies.
AUTHOR(S): Jordan, James E. (1); Morrissey, Margaret A. (1); Stahl, Gregory L. (1)
CORPORATE SOURCE: (1) Brigham and Women's Hospital, 75 Francis St., Boston, MA, 02115 USA
SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A338. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Complement is a major participant in post-ischemic reperfusion injury. The classical and alternative complement pathways have been extensively studied; however, the role of the **lectin complement pathway (LCP)** in inflammation has not been investigated since **inhibitors** of MBL have not been described. In order to delineate the participation of the **LCP**, we generated antibodies to rat **mannose binding lectin** (MBL). In this study, antibodies (Ab) were produced and characterized for potential use in further dissecting the role of the **LCP** in rat models of human disease. Polyclonal and monoclonal antibodies were produced in rabbits and mice using purified MBL isolated from rat sera by affinity chromatography and standard immunization techniques. All antibodies were screened using 2 different ELISA systems (binding to mannan or BSA coupled to N-acetyl-D-glucosamine; BSA-GlcNAc) to detect complement activation and deposition of C3. Monoclonal Ab P7E4 **inhibited** C3 deposition onto BSA-GlcNAc coated plates in a concentration-dependent manner with maximal **inhibition** (apprx80%) occurring at 10 mug/mL. Similarly, Fab fragments of the polyclonal antibody **inhibited** complement deposition in a concentration dependent manner. Western blot analysis was performed to determine the isoform(s) of rat MBL that the antibodies recognized. While the polyclonal Ab recognized multiple oligomers of A and C isoforms under non-reducing conditions, mAb P7E4 only recognized the A isoform. Similar results were obtained under reducing conditions in that the polyclonal Ab recognized both forms while only the A isoform was recognized by P7E4. These data confirm that the antibodies recognize rat **mannose binding lectin**, **inhibit** the function of MBL and may serve as useful reagents in studying the **lectin complement pathway** in rat models of human disease.

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polyclonal antibody **inhibited** complement deposition in a concentration dependent manner. Western blot analysis was performed to determine the isoform(s) of rat **MBL** that the antibodies recognized. While the polyclonal Ab recognized multiple oligomers of A and C isoforms under non-reducing conditions, mAb. . . recognized both forms while only the A isoform was recognized by P7E4. These data confirm that the antibodies recognize rat **mannose binding lectin, inhibit** the function of **MBL** and may serve as useful reagents in studying the **lectin complement pathway** in rat models of human disease.

L11 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 3
ACCESSION NUMBER: 2001:456188 CAPLUS
TITLE: Ulex europaeus agglutinin II (UEA-II) is a novel, potent inhibitor of complement activation
AUTHOR(S): Lekowski, Robert; Collard, Charles D.; Reenstra, Wende R.; Stahl, Gregory L.
CORPORATE SOURCE: Center for Experimental Therapeutics and Reperfusion Injury, Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Protein Sci. (2001), 10(2), 277-284
CODEN: PRCIEI; ISSN: 0961-8368
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Complement is an important mediator of vascular injury following oxidative stress. We recently demonstrated that complement activation following endothelial oxidative stress is mediated by **mannose-binding lectin** (**MBL**) and activation of the **lectin complement pathway**. Here, we investigated whether nine plant lectins which have a binding profile similar to that of **MBL** competitively **inhibit** **MBL** deposition and subsequent complement activation following human umbilical vein endothelial cell (HUVEC) oxidative stress. HUVEC oxidative stress (1% O2, 24 h) significantly increased Ulex europaeus agglutinin II (UEA-II) binding by 72.+-.9% compared to normoxic cells. UEA-II **inhibited** **MBL** binding to HUVEC in a concn.-dependent manner following oxidative stress. Further, **MBL** **inhibited** UEA-II binding to HUVEC in a concn.-dependent manner following oxidative stress, suggesting a common ligand. UEA-II (.ltoreq. 100 .mu.mol/L) did not attenuate the hemolytic activity, nor did it **inhibit** C3a des Arg formation from alternative or classical complement pathway-specific hemolytic assays. C3 deposition (measured by ELISA) following HUVEC oxidative stress was **inhibited** by UEA-II in a concn.-dependent manner (IC50 = 10 pmol/L). UEA-II **inhibited** C3 and **MBL** co-localization (confocal microscopy) in a concn.-dependent manner on HUVEC following oxidative stress (IC50 .apprxeq. 1 pmol/L). Finally, UEA-II significantly **inhibited** complement-dependent neutrophil chemotaxis, but failed to **inhibit** fMLP-mediated chemotaxis, following endothelial oxidative stress. These data demonstrate that UEA-II is a novel, potent **inhibitor** of human **MBL** deposition and complement activation following human endothelial oxidative stress.

REFERENCE COUNT: 29
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(1) Alencar, N; Mediators Inflamm 1999, V8, P107 CAPLUS
(2) Bless, N; Am J Physiol 1999, V276, PL57 CAPLUS
(3) Buerke, M; Journal of Pharmacology and Experimental Therapeutics 1998, V286, P429 CAPLUS
(4) Collard, C; Am J Pathol 2000, V156, P1549 CAPLUS
(5) Collard, C; Arterioscler Thromb Vasc Biol 1999, V19, P2623 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Complement is an important mediator of vascular injury following oxidative stress. We recently demonstrated that complement activation following endothelial oxidative stress is mediated by **mannose-binding lectin** (**MBL**) and activation of the **lectin complement pathway**. Here, we investigated whether nine plant lectins which have a binding profile similar to that of **MBL** competitively **inhibit** **MBL** deposition and subsequent complement activation following human umbilical vein endothelial cell (HUVEC) oxidative stress. HUVEC oxidative stress (1% O2, 24 h) significantly increased Ulex europaeus agglutinin II (UEA-II) binding by 72.+-.9% compared to normoxic cells. UEA-II **inhibited** **MBL** binding to HUVEC in a concn.-dependent manner following oxidative stress. Further, **MBL** **inhibited** UEA-II binding to HUVEC in a concn.-dependent manner following oxidative stress, suggesting a common ligand. UEA-II (.ltoreq. 100 .mu.mol/L) did not attenuate the hemolytic activity, nor did it **inhibit** C3a des Arg formation from alternative or classical complement pathway-specific hemolytic assays. C3 deposition (measured by ELISA) following HUVEC oxidative stress was **inhibited** by UEA-II in a concn.-dependent manner (IC50 = 10 pmol/L). UEA-II **inhibited** C3 and **MBL** co-localization (confocal microscopy) in a concn.-dependent manner on HUVEC following oxidative stress (IC50 .apprxeq. 1 pmol/L). Finally, UEA-II significantly **inhibited** complement-dependent neutrophil chemotaxis, but failed to **inhibit** fMLP-mediated chemotaxis, following endothelial oxidative stress. These data demonstrate that UEA-II is a novel, potent **inhibitor** of human **MBL** deposition and complement activation following human endothelial oxidative stress.

L11 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:420986 CAPLUS
DOCUMENT NUMBER: 133:57580
TITLE: Methods and products for regulating lectin complement pathway associated complement activation
INVENTOR(S): Stahl, Gregory L.; Collard, Charles D.
PATENT ASSIGNEE(S): Brigham and Women's Hospital, Inc., USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035483	A1	20000622	WO 1999-US29919	19991215

W: CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1998-112390 P 19981215

AB The invention relates to methods and products for regulating **lectin complement pathway** assocd. complement activation. The methods include both in vitro and in vivo methods for **inhibiting lectin complement pathway** assocd. complement activation. The methods are accomplished by contacting a mammalian cell having surface exposed **MBL** ligand with an effective amt. of a mannan binding lectin **inhibitor** to **inhibit lectin complement pathway** assocd. complement activation. The mannan binding lectin **inhibitor** may be administered to a subject to prevent cellular injury mediated by **lectin complement pathway** assocd. complement activation. The products of the invention include compns. of a mannan binding lectin **inhibitor**. The mannan binding lectin **inhibitor** is an isolated mannan binding lectin binding peptide that selectively binds to a human mannan binding lectin epitope and that **inhibits lectin complement pathway** assocd. complement activation. The products also include hybridoma cell lines and pharmaceutical compns.

REFERENCE COUNT: 4

REFERENCE(S):
(1) Endo; International Immunology 1996, V8(9), P1355 CAPLUS
(2) Endo; Journal of Immunology 1998, V161, P4924 CAPLUS
(3) Sato; International Immunology 1994, V6(4), P665 CAPLUS
(4) Thiel; Nature 1997, V386, P506 CAPLUS

AB The invention relates to methods and products for regulating **lectin complement pathway** assocd. complement activation. The methods include both in vitro and in vivo methods for **inhibiting lectin complement pathway** assocd. complement activation. The methods are accomplished by contacting a mammalian cell having surface exposed **MBL** ligand with an effective amt. of a mannan binding lectin **inhibitor** to **inhibit lectin complement pathway** assocd. complement activation. The mannan binding lectin **inhibitor** may be administered to a subject to prevent cellular injury mediated by **lectin complement pathway** assocd. complement activation. The products of the invention include compns. of a mannan binding lectin **inhibitor**. The mannan binding lectin **inhibitor** is an isolated mannan binding lectin binding peptide that selectively binds to a human mannan binding lectin epitope and that **inhibits lectin complement pathway** assocd. complement activation. The products also include hybridoma cell lines and pharmaceutical compns.

L11 ANSWER 10 OF 11 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000255148 MEDLINE
DOCUMENT NUMBER: 20255148 PubMed ID: 10793066
TITLE: Complement activation after oxidative stress: role of the lectin complement pathway.
AUTHOR: Collard C D; Vakeva A; Morrissey M A; Agah A; Rollins S A; Reenstra W R; Buras J A; Meri S; Stahl G L
CORPORATE SOURCE: Center for Experimental Therapeutics and Reperfusion Injury, Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA.
CONTRACT NUMBER: HL-03854 (NHLBI)
HL-52886 (NHLBI)
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (2000 May) 156 (5) 1549-56. Journal code: 3RS; 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000616
Last Updated on STN: 20000616
Entered Medline: 20000602

AB The complement system plays an important role in mediating tissue injury after oxidative stress. The role of **mannose-binding lectin (MBL)** and the **lectin complement pathway (LCP)** in mediating complement activation after endothelial oxidative stress was investigated. iC3b deposition on hypoxic (24 hours; 1% O(2))/reoxygenated (3 hours; 21% O(2)) human endothelial cells was attenuated by N-acetyl-D-glucosamine or D-mannose, but not L-mannose, in a dose-dependent manner. Endothelial iC3b deposition after oxidative stress was also attenuated in **MBL**-deficient serum. Novel, functionally **inhibitory**, anti-human **MBL** monoclonal antibodies attenuated **MBL**-dependent C3 deposition on mannan-coated plates in a dose-dependent manner. Treatment of human serum with anti-**MBL** monoclonal antibodies **inhibited** **MBL** and C3 deposition after endothelial oxidative stress. Consistent with our in vitro findings, C3 and **MBL** immunostaining throughout the ischemic area at risk increased during rat myocardial reperfusion in vivo. These data suggest that the **LCP** mediates complement activation after tissue oxidative stress. **Inhibition** of **MBL** may represent a novel therapeutic strategy for ischemia/reperfusion injury and other complement-mediated disease states.

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L11 ANSWER 11 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:395748 BIOSIS
DOCUMENT NUMBER: PREV199900395748

TITLE: Endothelial reoxygenation activates the lectin complement pathway: Inhibition with anti-human mannose binding lectin (MBL) therapy.
AUTHOR(S): Collard, C. D. (1); Agah, A. (1); Buras, J. A. (1); Reenstra, W. R. (1); Morrissey, M. M. (1); Stahl, G. L. (1)
CORPORATE SOURCE: (1) Center for Experimental Therapeutics and Reperfusion Injury, Dept. of Anesthesiology, Pain and Perioperative Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA USA
SOURCE: Molecular Immunology, (March April, 1999) Vol. 36, No. 4-5, pp. 278.
Meeting Info.: 7th European Meeting on Complement in Human Disease Helsinki, Finland June 17-20, 1999
ISSN: 0161-5890.
DOCUMENT TYPE: Conference .,
LANGUAGE: English
TI Endothelial reoxygenation activates the lectin complement pathway: Inhibition with anti-human mannose binding lectin (MBL) therapy.

=> s Stahl G?/au and collard C?/au
L12 57 STAHL G?/AU AND COLLARD C?/AU

=> s l12 and complement
L13 54 L12 AND COMPLEMENT

=> dup rem l13
PROCESSING COMPLETED FOR L13
L14 26 DUP REM L13 (28 DUPLICATES REMOVED)

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L14 ANSWER 1 OF 26 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001259476 MEDLINE
DOCUMENT NUMBER: 21136395 PubMed ID: 11238665
TITLE: A keratin peptide inhibits mannose-binding lectin.
AUTHOR: Montalto M C; Collard C D; Buras J A; Reenstra W R; McClaine R; Gies D R; Rother R P; Stahl G L
CORPORATE SOURCE: Department of Anesthesiology, Perioperative and Pain Medicine, Center for Experimental Therapeutics and Reperfusion Injury, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, USA.
CONTRACT NUMBER: F32 HL-103870 (NHLBI)
HL-03854 (NHLBI)
HL-56086 (NHLBI)
SOURCE: JOURNAL OF IMMUNOLOGY, (2001 Mar 15) 166 (6) 4148-53.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered Medline: 20010517

AB Complement plays a significant role in mediating endothelial injury following oxidative stress. We have previously demonstrated that the lectin complement pathway (LCP), which is initiated by deposition of the mannose-binding lectin (MBL), is largely responsible for activating complement on endothelial cells following periods of oxidative stress. Identifying functional inhibitors that block MBL binding will be useful in characterizing the role of the LCP in disease models. The human cytokeratin peptide SFGSGFGGGY has been identified as a molecular mimic of N-acetyl-D-glucosamine (GlcNAc), a known ligand of MBL. Thus, we hypothesized that this peptide would specifically bind to MBL and functionally inhibit the LCP on endothelial cells following oxidative stress. Using a BIAcore 3000 optical biosensor, competition experiments were performed to demonstrate that the peptide SFGSGFGGGY inhibits binding of purified recombinant human MBL to GlcNAc in a concentration-dependent manner. Solution affinity data generated by BIAcore indicate this peptide binds to MBL with an affinity (K(D)) of 5 x 10(-5) mol/L. Pretreatment of human serum (30%) with the GlcNAc-mimicking peptide (10-50 microg/ml) significantly attenuated MBL and C3 deposition on human endothelial cells subjected to oxidative stress in a dose-dependent manner, as demonstrated by cell surface ELISA and confocal microscopy. Additionally, this decapeptide sequence attenuated complement-dependent VCAM-1 expression following oxidative stress. These data indicate that a short peptide sequence that mimics GlcNAc can specifically bind to MBL and functionally inhibit the proinflammatory action of the LCP on oxidatively stressed endothelial cells.

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